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(54) Tüle: NOVEL 1,2-BENZOTHIAZEPINES HAVING ACTIV TAUROCHOLATB UPTAKB	NOVEL 12-BENZOTHIAZZENIBS HAVING ACTIVITY AS INHIBITORS OF ILEAL BILE ACID TRANSPORT AND TAUROCHOLATE UPTAKE

# FOR THE PURPOSES OF INFORMATION ONLY

Novel 1.2-benzothiazapinea, derivatives and analoga theroof, pharmaceutical compositions containing them, and their use in medicine, particularly in the prophylasta and/or teament of hyperlipidemic diseases, conditions and/or disordem, such as those associated with alterorediconts and/or hyperholestron-lenia.

(57) Abstract

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# NOVEL 1,2-BENZOTHIAZEPINES HAVING ACTIVITY AS INHIBITORS OF ILEAL BILE ACID TRANSPORT AND TAUROCHOLATE UPTAKE

#### Field of the Invention

The present invention relates to novel 1,2-benzothiazepines, derivatives and analogs thereof, pharmaceutical compositions containing them, and their use in medicine, particularly in the prophylaxis and/or treatment of hyperlipidemic diseases, conditions and/or disorders, such as those associated with atherosclerosis and/or hypercholesterolemia, in marnmals.

#### Description of Related Art

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It is well-settled that hyperlipidemic conditions associated with elevated concentrations of total cholesterol and low-density lipoprotein ("LDL") cholesterol are major risk factors for coronary heart disease and particularly atherosclerosis. Interfering with the circulation of bile acids within the lumen of the intestinal tract is found to reduce the levels of serum cholesterol in a causal relationship. Epidemiological data has accumulated which indicates such reduction leads to an improvement in the disease state of atherosclerosis. Stedronsky, "Interaction Of Bile Acids And Cholesterol With Nonsystemic Agents Having Hypocholesterolemic Properties," Biochimica et Biophysica Acta, 1210 (1994) 255-287, discusses the biochemistry, physiology and known active agents relating to bile acids and cholesterol.

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interruption of the enterohepatic circulation of bile acids in humans in Heubi, J.E., et al., "Primary Bile Acid Malabsorption: Defective In Vitro Iteal Active Bile Acid Transport", Gastroenterology, 1982:83:804-11.

Pathophysiologic alterations are shown to be consistent with

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In fact, cholestyramine binds the bile acids in the intestinal tract, thereby interfering with their normal enterohepatic circulation. Reihner, E. et al, in "Regulation of Hepatic Cholesterol Metabolism In Humans: Stimulatory Effects Of Cholestyramine On HMG-CoA Reductase Activity And Low

5 Density Lipoprotein Receptor Expression In Gallstone Patients", <u>Journal of Lipid Research</u>, Volume 31, 1990, 2219-2226. This results in an increase in liver bile acid synthesis by the liver using cholesterol as well as an upregulation of the liver LDL receptors which enhances clearance of cholesterol and decreases serum LDL cholesterol levels. Suckling el al,

"Cholesterol Lowering And Bile Acid Excretion In The Hamster With Cholestyramine Treatment", <u>Atherosclerosis</u>, 89(1991) 183-190), also discloses the results of cholestyramine treatment to lower serum cholesterol levels.

In another approach to the reduction of recirculation of bile acids, the lieal bile acid transport system is a putative pharmaceutical target for the treatment of hypercholesterolemia based on an interruption of the enterohepatic circulation with specific transport inhibitors. Kramer, et al, "Intestinal Bile Acid Absorption", The Journal of Biological Chemistry, Vol. 268, No. 24, Issue of August 25, pp. 18035-18046, 1993.

20 In a series of patent applications, Hoechst Aktiengesellschaft discloses polymers of various naturally occurring constituents of the enterohepatic circulation system and their derivatives, including bile acid, which inhibit the physiological bile acid transport with the goal of reducing the LDL cholesterol level sufficiently to be effective as pharmaceuticals and, in particular for use as hypocholesterolemic agents. See, e.g., Canadian Patent Application Nos. 2,025,294; 2,078,588; 2,085,782; and 2,085,830; and EP Application Nos. 0

In vitro bile acid transport inhibition is disclosed to show hypolipidemic activity in The Wellcome Foundation Limited disclosure of the

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world patent application number WO 93/16055 for "Hypolipidemic Benzothiepine Compounds".

Selected benzothiepines are disclosed in world patent application number WO93/321146 for numerous uses including fatty acid metabolism and coronary vascular diseases.

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Additional benzothiepines for use as hypolipidemic agents are disclosed in WO97/33882 and U.S. Patent 5,994,391.

Other selected benzothiepines are known for use as hypolipaemic and hypocholesterolaemic agents, especially for the treatment or prevention of atherosclerosis as disclosed by application Nos. EP 508425, FR 2661676, and WO 92/18462, each of which is limited by an amide bonded to the carbon adjacent the phenyl ring of the fused bicyclo benzothiepine ring.

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WO96/16051 published May 30, 1996 describes certain 1,5-benzothiazepines as useful in the treatment of hypertipidemic conditions.
WO96/05188 published February 22, 1996 describes certain 1,4-benzothiazepines as useful in the treatment of hyperlipidemic conditions.

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Additional benzothiazepines are discussed in the references set forth below. These references either do not disclose a specific utility or disclose a different utility than the present invention.

Orahovats et al., "A Ring Enlargement From Seven- To Ten-Membered-Ring Sulfonamide Derivatives", <u>Helv. Chim. Acta.</u> vol. 79, pp. 1121-1128 (1996) describes 4,5-dihydro-7,8-dimethoxy-1,2-benzothiazepine-3-one-1,1-dioxide. Katrizky et al., "Preparation Of 6-, 7- and 8-Membered Sultams By Friedel-Crafts Cyclization Of 20-Phenylalkanesulfamoyl Chlorides", <u>Org. Prep. Proced. Int.</u>, vol. 24(4), pp. 463-467 (1992) describes 2,3,4,5-tetrahydro-1,2-benzothiazepine-1,1-dioxide and 2,3,4,5-tetrahydro-2-butyl-1,2-benzothiazepine-1,1-dioxide for possible use as an anticonvulsant, diuretic or sedative.

Beckwith et al., "Iododediazoniation Of Arenediazonium Salts Accompanied By Aryl Radical Ring Closure", <u>I. Org. Chem.</u> vol. 52, pp. 1922-1930 (1987) describes 2,3,4,5-tetrahydro-2-allyl-1,2-benzothiazepine-1,1-dioxide.

Stassinopolou et al., ""BC NMR Spectra Of Berzothiazepine, Berzothiazone and Berzosulphonamide N-substituted Derivatives", <u>Org.</u>

<u>Magn. Reson.</u>, vol. 21(3), pp. 187-189 (1983), describes certain N-substituted 4,5-dihydro-7,8-dimethoxy-1,2-berzothiazepine-3-one-1,1-dioxides.

Tamura et al., "Novel Conversions Of Benzo[b]thiophen-3(2H)-ones

10 Into 1,2-Benzisothiazole And Tetrahydro-1,2-benzothiazepin-5-One Systems
Via Sulphimide Intermediates", I. Chem. Soc., Perkin Trans. I. vol. 12, pp.

2830-2834 (1980) describes 2,3,4,5-tetrahydro-2-tosyl-4-methyl-1,2benzothiazepine-5-one-1,1-dioxide.

Catsoulacos et al., "Synthesis Of Some N-Substituted 4,5-Dibydro-7,8-dimethoxybenzothiazepin-3-one 1,1-Dioxides, <u>I. Hetero, Chem.</u> vol. 13(6), pp. 1309-1314 (1976) describes 4,5-dibydro-7,8-dimethoxy-1,2-benzothiazepine-3-one-1,1-dioxide and certain 4,5-dibydro-2-(phenyl, substituted phenyl or pyridyl)-7,8-dimethoxy-1,2-benzothiazepine-3-one-1,1-dioxides having anti-inflammatory and central nervous system activity.

Pangiotopoulos et al., "N(p-Bromopheny!)-4,5-Dihydro-7,8-Dimethoxy Benzothiazepine-3-One 1,1-Dioxide C,H,H,BrNO,S", <u>Cryst. Struct. Comm.</u>, vol. 9, pp. 313-320 (1980) describes 4,5-dihydro-2-(4-bromopheny!)-7,8-dimethoxy-1,2-benzothiazepine-3-one-1,1-dioxide.

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Catsoulacos et al., "Thiazo Compounds: Derivatives Of 4,5-Dihydro-7,8-Dimethoxybenzothiazepin-3-one 11-Dioxides", <u>I. Chem. Eng. Data.</u> vol. 22(3), pp. 353-354 (1977) describes 4,5-dihydro-2-(ethyl, n-propyl or isopropyl)-7,8-dimethoxy-1,2-benzothiazepine-3-one-1,1-dioxide.

Camoutsis et al., "N-Substituted 4,5-Dihydro-1,2-benzothiaepin-3-one 1,1-Dioxide", L. Hetero, Chem., vol. 17(5), pp. 1135-1136 (1980) describes

one-1, 1-dioxides. certain 4,5-dihydro-2-(3- or 5-pyridyl)-7,8-dimethoxy-1,2-benzothiazepine-3-

are described as lipoxygenase inhibitors useful in the treatment of inflammatory and allergic conditions generically encompass certain benzothiazepine compounds. These derivatives U.S. Patent No. 5,350,761 describes hydroxylamine derivatives that

heterocyclyl)alkyl)-benzothiazepines as useful for controlling micturition. containing-heterocyclyl)alkyl)benzothiazepines and aralkyl-(N-containing-WO98/02432 published January 22, 1998 describes certain 5-(aryl-(N.

5 sulfonylamino-substituted benzothiazepines as inhibitors of the enzyme cyclooxygenase II WO97/03953 published February 6, 1997 describes certain

compounds are identified as kappa receptor agonists useful as analgesics and diuretics and for the treatment of cerebral ischaemia benzothiazepines substituted with azacyclic condensed piperazines. These WO95/21843 published August 17, 1995 describes certain

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benzothiazepine-5-ones useful as muscle relaxants. EP338331 published October 25, 1989 describes certain 2-

#### Summary of the Invention

20 that are effective agents for the prophylaxis and/or treatment of hyperlipidemic diseases, conditions and/or disorders. A first aspect of the invention comprises novel 1,2- benzothiazepines

the prophylaxis and/or treatment of hyperlipidemic diseases, conditions and/or compositions comprising the novel 1,2- benzothiazepines that are suitable for A second aspect of the invention comprises pharmaceutical

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and/or treatment of hyperlipidemic diseases, conditions and/or disorders A third aspect of the invention comprises methods for the prophylaxis

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effective amount of one of the novel 1,2- benzothiazepines. comprising administering to a subject a prophylactically or therapeutically

novel 1,2-benzothiazepines of the present invention A fourth aspect of the invention comprises methods of making the

specification of this application. Additional aspects of the invention are discussed throughout the

### Detailed Description of the Invention

the art in practicing the present invention. This detailed description, The following detailed description is provided to aid those skilled in

- 15 ö these primary references, are herein incorporated by reference in their references cited herein, including the contents of the references cited within however, should not be construed to unduly limit the present invention as scope of the present inventive discovery. The contents of each of the made by those of ordinary skill in the art without departing from the spirit or modifications and variations in the embodiments discussed herein can be
- Accordingly, the present invention provides compounds

corresponding to the structure of Formula (I):

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wherein:

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q is an integer from 1 to 4;

R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of hydrogen and hydrocarbyl, wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus;

R<sup>3</sup> and R<sup>4</sup> are independently selected from the group consisting of hydrogen; hydrocarbyl; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; and -SO<sub>3</sub>R<sup>9</sup>; or

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 $\rm R^3$  and  $\rm R^4$  together form =0; =NOR  $^9$  , =S; =NNR  $^9\rm R^{10}$  ; =NR  $^9$  , or =CR  $^{11}\rm R^{12}$  ,

wherein R<sup>9</sup> and R<sup>10</sup> are independently selected from the group consisting of hydrogen; hydrocarbyl; amino; and hydrocarbylamino; wherein said hydrocarbyl moicties may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl moieties optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; and

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wherein R<sup>11</sup> and R<sup>12</sup> are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; hydrocarbyl; -OR<sup>9</sup>, -NR<sup>9</sup>R<sup>10</sup>, -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; and -SO<sub>3</sub>R<sup>9</sup>; wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; or R<sup>11</sup> and R<sup>12</sup> together with the carbon atom to which they are

 $R^5$  and  $R^6$  are independently selected from the group consisting of

attached form a cyclic ring; and

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hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; -OR<sup>9</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; and -SO<sub>3</sub>R<sup>9</sup>;

wherein the R<sup>5</sup> and R<sup>6</sup> radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; -NO2; -CN; oxo; hydrocarbyl; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO<sub>2</sub>R<sup>13</sup>; -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>; -C(O)NR<sup>13</sup>R<sup>14</sup>; -C(O)OM; -COR<sup>13</sup>; -NR<sup>13</sup>C(O)R<sup>1</sup>, -NR<sup>13</sup>C(O)NR<sup>14</sup>R<sup>15</sup>; -NR<sup>13</sup>CO<sub>2</sub>R<sup>15</sup>; -NR<sup>13</sup>CO<sub>3</sub>R<sup>15</sup>; -NR<sup>13</sup>CO<sub>3</sub>R

NR<sup>13</sup>SO<sub>2</sub>NR<sup>14</sup>R<sup>15</sup>, -PR<sup>13</sup>R<sup>14</sup>, -P(O)R<sup>13</sup>R<sup>14</sup>, -P<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>-</sup>; .

P(OR<sup>13</sup>)OR<sup>14</sup>, -S<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A<sup>-</sup>; and -N<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>-</sup>; wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; and

wherein R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> are independently selected from hydrogen and hydrocarbyl, wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by

said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; or wherein R<sup>13</sup> and R<sup>14</sup> together with the nitrogen atom to which they

are attached form a mono- or polycyclic heterocycly! that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

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wherein  $R^{14}$  and  $R^{15}$  together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein A is a pharmaceutically acceptable anion, and M is a

R4 and R6 together represent a bond; and

 $\mathbb{R}^{N}$  is selected from the group consisting of hydrogen and

or more heteroatoms independently selected from the group consisting of hydrocarbyl optionally may have one or more carbon atoms replaced by one hydrocarbyl, wherein said hydrocarbyl may be optionally substituted with oxygen, nitrogen, sulfur and phosphorus; one or more groups comprising one or more heteroatoms, and wherein said

5  $NR^{1}C(0)R^{13}$ ; -C(0) $NR^{13}R^{14}$ ; -C(0)OM; -COR  $^{13}$ ; -S(0) $_{II}NR^{13}R^{14}$ ; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO<sub>2</sub>R<sup>13</sup>; -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -S(O)2R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -S<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A; consisting of hydrogen; halogen; -CN; -NO2; hydrocarbyl; -OR  $^{13}$ ; one or more  $\mathbb{R}^{X}$  radicals are independently selected from the group

N+R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A-; -PR<sup>13</sup>R<sup>14</sup>; -P(O)R<sup>13</sup>R<sup>14</sup>; -P+R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A-; amino optionally may have one or more carbon atoms replaced by one or more groups comprising one or more heteroatoms, and wherein said hydrocarby wherein said hydrocarbyl may be optionally substituted with one or more acid residue; peptide residue; polypeptide residue; and carbohydrate residue,

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20 nitrogen, sulfur and phosphorus; and heteroatoms independently selected from the group consisting of oxygen

wherein n is 0, 1 or 2; and

wherein R13, R14, R15, A, and M are as defined above; or

provided that at least one of R1, R2, R3, R4, R5, and R6 is a a pharmaceutically acceptable salt, solvate, or prodrug thereof; and

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radical other than hydrogen or alkyl; and

radical other than heterocycylalkyl. provided that when R<sup>2</sup> or R<sup>6</sup> is aryl, the other of R<sup>2</sup> and R<sup>6</sup> is a

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Formula I wherein: A preferred class of compounds comprises those compounds of

q is an integer from 1 to 4;

alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; hydrogen; alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl;  $\mathbb{R}^1$  and  $\mathbb{R}^2$  are independently selected from the group consisting of

5 form C<sub>3</sub>-C<sub>10</sub> cycloalkyl or C<sub>3</sub>-C<sub>10</sub> cycloalkenyl;  $\mathbb{R}^1$  and  $\mathbb{R}^2$  taken together with the carbon to which they are attached

alkylaryl; and (polyalkyl)aryl; or

aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; wherein the R<sup>1</sup> and R<sup>2</sup> alkyl; cycloalkyl; alkenyl; cycloalkenyl;

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20 CO2R9; and -CONR9R10; and consisting of -CN; halogen; oxo; -OR9; -NR9R10; -N+R9R10RWA; -SR9; may be substituted with one or more radicals selected from the group -S'R'R\"A; -PR\"R\"\; -P\"R\"R\"R\"\A; -S(O)R\"; -SO2R\"; -SO3R\"; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally

aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; wherein the  $\mathbb{R}^1$  and  $\mathbb{R}^2$  alkyl; cycloalkyl; alkenyl; cycloalkenyl;

consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; SO-; -SO2-; -S $^+R^9A^-$ ; -PR $^9$ -; -P(O)R $^9$ -; -P $^+R^9R^{10}A^-$ ; or phenylene; and may have one or more carbons replaced by -O-; -NR  $^9$  -; -N $^+$ R  $^9$ R  $^10$ A--; -S-; heterocyclyloxyalkynyi; alkylaryl; and (polyalkyl)aryl radicals optionally wherein  $R^9$ ,  $R^{10}$ , and  $R^W$  are independently selected from the group

heterocyclyl; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl; carboxyheterocyclyl; amino; alkylamino; carboxyalkylamino; carboxyalkyl; alkoxyalkyl; carboalkoxyalkyl; carboxyaryl; alkoxyalkylamino; and acyl; or

 $\mathbb{R}^3$  and  $\mathbb{R}^4$  are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; -OR $^9$ ; -NR $^9$ R $^{10}$ ; wherein A is a pharmaceutically acceptable anion; and SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; and -SO<sub>3</sub>R<sup>9</sup>; or

 $\mathbb{R}^3$  and  $\mathbb{R}^4$  together form =0; =NOR $^9$ ; =S; =NNR $^9$ R $^1$ 0; =NR $^9$ ; or -CR11R12;

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cyanoalkyi; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>9</sup>; -CO<sub>2</sub>R<sup>9</sup>; consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkynyl; aryl; wherein  $R^{11}$  and  $R^{12}$  are independently selected from the group heterocyclyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; carboalkoxyalkyl; cycloalkyl; cycloalkenyl; haloalkyl; hydroxyalkyl;

 $R^{11}$  and  $R^{12}$  together with the carbon atom to which they are attached form a cyclic ring; and and -CONR9R10; or

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wherein R9 and R10 are as defined above; and

hydrogen; alkyi; cycloalkyi; alkenyi; alkynyi; aryi; heterocyclyi; quaternary  $\mathbb{R}^5$  and  $\mathbb{R}^6$  are independently selected from the group consisting of heterocyclyl;  $-OR^9$ ;  $-SR^9$ ;  $-S(O)R^9$ ;  $-SO_2R^9$ ; and  $-SO_3R^9$ ; 2

substituted with one or more radicals independently selected from the group heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; -OR 13; -NR 13R 14; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary SR<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; wherein the  $\rm R^5$  and  $\rm R^6$  alkyl; cycloalkyl; alkenyl; aryl; aryl; heterocyclyl; and quaternary heterocyclyl radicals optionally may be consisting of halogen; -CN; -NO2; oxo; alkyl; polyalkyl; haloalkyl;

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 $CO_2R^{13}$ ; -OM; -SO2OM; -SO2NR<sup>13</sup>R<sup>14</sup>; -C(O)NR<sup>13</sup>R<sup>14</sup>; -C(O)OM; -COR<sup>13</sup>; -NR<sup>13</sup>C(O)R"; -NR<sup>13</sup>C(O)NR"R"; -NR"CO,R"; -OC(O)R"; - $NR^{13}SO_2NR^{14}R^{13}, -PR^{13}R^{14}; -P(O)R^{13}R^{14}; -P^{+}R^{13}R^{14}R^{15}A^{\frac{1}{2}}; -P^{-}R^{13}R^{14}R^{15}A^{\frac{1}{2}}; -P^{-}R^{13}R^{14}R^{15}A^{\frac{1}{2}}; -P^{-}R^{13}R^{14}R^{15}A^{\frac{1}{2}}; -P^{-}R^{13}R^{14}R^{15}R^{\frac{1}{2}}; -P^{-}R^{13}R^{14}R^{\frac{1}{2}}; -P^{-}R^{13}R^{14}R^{\frac{1}{2}}; -P^{-}R^{13}R^{14}R^{15}R^{\frac{1}{2}}; -P^{-}R^{13}R^{14}R^{15}R^{1$ OC(0)NR<sup>13</sup>R<sup>14</sup>; -NR<sup>13</sup>SOR<sup>14</sup>; -NR<sup>13</sup>SO<sub>3</sub>R<sup>14</sup>; -NR<sup>13</sup>SONR<sup>14</sup>R<sup>15</sup>;

P(OR13)OR14; -S+R13R14A; and -N+R13R14R15A; and

from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; heterocyclyl; -OR<sup>7</sup>; -NR<sup>7</sup>R<sup>8</sup>; -SR<sup>7</sup>; -S(O)R<sup>7</sup>; -SO<sub>2</sub>R<sup>7</sup>; -SO<sub>2</sub>R<sup>7</sup>; -CO<sub>2</sub>R<sup>7</sup>; alkenyi; alkynyi; aryi; heterocyciyi; arylalkyi; heterocyclylalkyi; quaternary CONR 7R3; -N+R7R8R9A:, -P(O)R7R8; -PR7R8; -P+R7R8R9A; and wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, optionally may be further substituted with one or more radicals selected aikenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R3 and R6 radicals P(O)(OR7)OR8; and 2

N^R7R8A:; -S.; -SO-; -SO2:; -S^R7A:; -PR7.; -P(0)R7-; -P\*R7R8A:; or wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R3 and R6 radicals optionally may have one or more carbons replaced by -O-; -NR<sup>7</sup>-; -

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phenylene; and ន

consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and wherein R 13, R 14, and R 15 are independently selected from the wherein R7 and R8 are independently selected from the group

alkenyl; alkynyl; aryl; heterocyclyl; quatemary heterocyclyl; arylalkyl; group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; heterocyciylalkyl; quatemary heterocyciylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminoalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or aminocarbonylalkyl; alkylaminocarbonylalkyl;

oxo, carboxy, and quaternary salts; or substituted with one or more radicals selected from the group consisting of are attached form a mono- or polycyclic heterocyclyl that is optionally wherein R13 and R14 together with the nitrogen atom to which they

are attached form a cyclic ring; and wherein  $\mathbb{R}^{14}$  and  $\mathbb{R}^{15}$  together with the nitrogen atom to which they

alkylheterocyclylalkyl; alkylammoniumalkyl; aminoalkyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; wherein the  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  alkyl; haloalkyl; cycloalkyl;

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halogen; -CN; sulfo; oxo; alkyl; haloalkyl; hydroxyalkyl; sulfoalkyl; substituted with one or more radicals selected from the group consisting of carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be aminocarbonylalkyl; alkylaminocarbonylalkyl;

ᅜ alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary S<sup>+</sup>R<sup>9</sup>R <sup>10</sup>A-; and carbohydrate residue; and CONR<sup>9</sup>R<sup>10</sup>; -SO<sub>2</sub>NR<sup>9</sup>R<sup>10</sup>; -PO(OR <sup>16</sup>)OR <sup>17</sup>; -P<sup>9</sup>R <sup>10</sup>; -P<sup>+</sup>R<sup>9</sup>R <sup>10</sup>R <sup>11</sup>A-; -N+R9R10RWA;-SR16;-S(O)R9;-SO2R9;-SO3R16;-CO2R16;heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; -OR 16; -NR 9R 10;

arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminoalkyl; wherein the  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  alkyl; haloalkyl; cycloalkyl;

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residue; amino acid residue; peptide residue; or polypeptide residue; and have one or more carbons replaced by -O-; -NR\*-; -N $^+$ R $^9$ R $^{10}$ A-; -S-; -SO-; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may  $-SO_{2^{+}}\cdot S^{+}R^{9}A\cdot ;\cdot PR^{9}\cdot ;\cdot P^{+}R^{9}R^{10}A\cdot ;\cdot P(0)R^{9}\cdot ; phenylene; carbohydrate$ wherein  $\mathbb{R}^{16}$  and  $\mathbb{R}^{17}$  are independently selected from the group

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consisting of R and M; and

alkynyl; aralkyl; and heterocyclylalkyl; and  $\mathbb{R}^{N}$  is selected from the group consisting of hydrogen; alkyl; alkenyl; wherein R, R, R, R, R, R, and A are as defined above; and wherein M is a pharmaceutically acceptable cation; and

heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy; -OR 13; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary consisting of hydrogen; halogen; -CN; -NO2; alkyl; cycloalkyl; polyalkyl; one or more  $\mathbb{R}^{X}$  radicals are independently selected from the group

ᅜ 5 polypeptide residue; and carbohydrate residue; S(O)nNR 13R 14; -NR 13R 18; -NR 18OR 14; -N+R 13R 14R 15A; -PR 13R 14  $\label{eq:coring} {\tt NR^{14}C(O)R^{13}; -C(O)NR^{13}R^{14}; -C(O)OM; -COR^{13}; -OR^{18}; -}$ NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO<sub>2</sub>R<sup>13</sup>; -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>;  ${\tt NR}^{13}{\tt R}^{14}; -{\tt SR}^{13}; -{\tt S}({\tt O}){\tt R}^{13}; -{\tt S}({\tt O}){\tt 2R}^{13}; -{\tt SO}_{\tt 3R}^{13}; -{\tt S}^{+}{\tt R}^{13}{\tt R}^{14}{\tt A}; -$ -P(O)R $^{13}$ R $^{14}$ ; -P $^{+}$ R $^{13}$ R $^{14}$ R $^{15}$ A $^{-}$ ; amino acid residue; peptide residue;

20 NR<sup>9</sup>R<sup>10</sup>; N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>W</sup>A; -SR<sup>16</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>16</sup>; acyloxy radicals optionally may be further substituted with one or more alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; radicals selected from the group consisting of halogen; -CN; oxo; -OR 16, wherein the R\* alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl;

 $P^+R^9R^{11}R^{12}A^-$ ;  $-S^+R^9R^{10}A^-$ ; and carbohydrate residue; and substituted with one or more radicals selected from the group consisting of CO2R<sup>16</sup>; -CONR<sup>9</sup>R<sup>10</sup>; -SO2NR<sup>9</sup>R<sup>10</sup>; -PO(OR<sup>16</sup>)OR<sup>17</sup>; -P<sup>9</sup>R<sup>10</sup>; wherein the R\* quaternary heterocyclyl radical optionally may be

25  $SO_2OM; -SO_2NR^{13}R^{14}; -C(O)NR^{13}R^{14}; -C(O)OM; -COR^{13};$ SO2R<sup>13</sup>; -SO3R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO2R<sup>13</sup>; OM; heterocyclylalkyl; polyether; -OR $^{13}$ ; -NR $^{13}$ R $^{14}$ ; -SR $^{13}$ ; -S(O)R $^{13}$ ; hydroxyalkyi; alkenyi; alkynyl; aryl; heterocyclyl; arylalkyi; halogen; -CN; -NO2; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl;

wherein the R<sup>X</sup> radicals comprising carbon optionally may have one or more carbons replaced by -O.; -NR <sup>13</sup>; -N<sup>+</sup>R <sup>13</sup>R <sup>14</sup>A·; -S·; -SO.; -SO<sub>2</sub>; -S<sup>+</sup>R <sup>13</sup>A·; -PR <sup>13</sup>; -P(O)R <sup>13</sup>; -P(D)R <sup>13</sup>; -P(D)Peptide residue; carbohydrate amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; polyether; or polyalkyl; wherein said phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; and polyalkyl optionally may have one or more carbons replaced by -O.; -NR <sup>9</sup>; -N<sup>+</sup>R <sup>9</sup>R <sup>10</sup>A·; or -P(O)R<sup>9</sup>; and

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wherein R<sup>18</sup> is selected from the group consisting of alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and

heterocyclylalkoxycarbonyl; and

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wherein the R<sup>11</sup> alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; NO; oxo; -OR?; -NR?R<sup>10</sup>, -N<sup>†</sup>R?R<sup>11</sup>ZA; -SR?; -S(O)R³; -SO2R³; -SO3R³; -CO2R?; -CONRRR<sup>10</sup>; -SO2OM; -SO2NR<sup>9</sup>R<sup>10</sup>; -P(OR<sup>13</sup>)OR<sup>14</sup>; -PO(OR<sup>16</sup>)OR<sup>17</sup>; and -C(O)OM;

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a pharmaceutically acceptable salt, solvate, or prodrug thereof.

In the various embodiments of the invention, R<sup>5</sup> and R<sup>6</sup> preferably are independently selected from the group consisting of H; aryl;

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heterocyclyl; and quaternary heterocyclyl;

wherein the R<sup>5</sup> and R<sup>6</sup> aryl; heterocyclyl; and quaternary heterocyclyl; radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; -CN;

- 5 -NO2; oxo; alkyi; polyalkyi; haloakyi; hydroxyakyi; cycloalkyi; alkenyi; alkynyi; aryi; heterocyclyi; quaternary heterocyclyi; aryialkyi; heterocyclyialkyi; polyether; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO<sub>2</sub>R<sup>13</sup>; -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>OM; -CO)NR<sup>13</sup>R<sup>14</sup>; -C(O)NR<sup>13</sup>R<sup>14</sup>; -C(O)OM; -COR<sup>13</sup>; -

- 20 heterocyclyl; -OR<sup>7</sup>; -NR<sup>7</sup>R<sup>8</sup>; -SR<sup>7</sup>; -S(O)R<sup>7</sup>; -SO<sub>2</sub>R<sup>7</sup>; -SO<sub>3</sub>R<sup>7</sup>; -CO<sub>2</sub>R<sup>7</sup>; -CONR<sup>7</sup>R<sup>8</sup>; -N<sup>4</sup>R<sup>7</sup>R<sup>8</sup>P<sup>8</sup>A<sup>2</sup>; -P(O)R<sup>8</sup>; -P<sup>8</sup>R<sup>9</sup>A<sup>2</sup>; and -P(O)(OR<sup>7</sup>)OR<sup>8</sup>; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl,

alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl,

25 heterocyclylalkyl, and polyether substituents of the R<sup>5</sup> and R<sup>5</sup> radicals

optionally may have one or more carbons replaced by -O-; -NR<sup>7</sup>-;

N<sup>+</sup>R, <sup>7</sup>R, <sup>8</sup>A-; -S-; -SO-; -SO<sub>2</sub>; -S<sup>+</sup>R, <sup>7</sup>A-; -PR, <sup>7</sup>-; -P(O)R<sup>7</sup>-; -P<sup>+</sup>R, <sup>7</sup>R, <sup>8</sup>A-; or

phenylene; and

wherein  $\mathbb{R}^7$  and  $\mathbb{R}^8$  are independently selected from the group

alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; wherein  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  are independently selected from the

heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl;

alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl;

are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or wherein R<sup>13</sup> and R<sup>14</sup> together with the nitrogen atom to which they

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are attached form a cyclic ring; and wherein  $\mathbb{R}^{14}$  and  $\mathbb{R}^{15}$  together with the nitrogen atom to which they

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radicals optionally may be substituted with one or more radicals selected alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; arylalkyl; heterocyclylalkyl; quatemary heterocyclylalkyl; alkylarylalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; wherein the R  $^{13}$ , R  $^{14}$ , and R  $^{15}$  alkyl; haloalkyl; cycloalkyl;

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-\$03R<sup>16</sup>; -CO2R<sup>16</sup>; -CONR<sup>9</sup>R<sup>10</sup>; -SO2NR<sup>9</sup>R<sup>10</sup>; -PO(OR<sup>16</sup>)OR<sup>17</sup>; arylalkyl; heterocyclylalkyl; quatemary heterocyclylalkyl; alkylarylalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl;  $PR^9R^{10}$ ;  $P^+R^9R^{10}R^{11}A$ ;  $S^+R^9R^{10}A$ ; and carbohydrate residue; and guanidinyl; -OR<sup>16</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>W</sup>A<sup>-</sup>; -SR<sup>16</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; wherein the  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  alkyl; haloalkyl; cycloalkyl;

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 $N^{\dagger}R^{9}R^{10}A:$ ; -S-; -SO-; -SO<sub>2</sub>-; -S<sup>†</sup>R<sup>9</sup>A-; -PR<sup>9</sup>-; -P<sup>†</sup>R<sup>9</sup>R<sup>10</sup>A-; -P(O)R<sup>9</sup>-; radicals optionally may have one or more carbons replaced by -O-; -NR9-; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl;

polypeptide residue; and phenylene; carbohydrate residue; amino acid residue; peptide residue; or

consisting of R9 and M; and wherein  $\mathbb{R}^{16}$  and  $\mathbb{R}^{17}$  are independently selected from the group

wherein M is a pharmaceutically acceptable cation; and

5 for the compounds of Formula I. wherein R9, R10, R11, R12, Rw, and A are as previously set forth above

More preferably, R5 or R6 has the formula -Ar-(R,),

is an integer from 0 to 5;

5 quinolinyl; isoquinolinyl; quinoxalinyl; imidazolyl; pyrazolyl; oxazolyl pyridyl; piperazinyl; piperonyl; pyrrolyl; naphthyl; furanyl; anthracenyl; benzoimidazolyl; benzoxazolyl; benzothiazolyl; and benzoisothiazolyl; and isoxazolyl; pyrimidinyl; thiazolyl; triazolyl; isothiazolyl; indolyl; Ar is selected from the group consisting of phenyl; thiophenyl;

25 20 OM;  $-SO_2OM$ ;  $-SO_2NR^{13}R^{14}$ ;  $-C(O)NR^{13}R^{14}$ ; -C(O)OM;  $-COR^{13}$ ; arylaikyl; heterocyclylaikyl; polyether; -OR 13; -NR 13R 14; -SR 13; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; of halogen; -CN; -NO2; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; NR"SO,NR"R"; -P(O)R 13R 14; -PR 13R 14; -P+R 13R 14R 15A; -OC(O)NR13R14; -NR13SOR14; -NR13SO,R14; -NR13SONR14R15; -NR13C(O)R14; -NR13C(O)NR14R15; -NR13CO2R14; -OC(O)R13; -S(O)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO<sub>2</sub>R<sup>13</sup>; one or more RY are independently selected from the group consisting

P(OR 13)OR 14; -S+R13R14A; and -N+R13R14R15A; and

may be further substituted with one or more radicals selected from the group  $\mathsf{heterocyclyl}; -\mathsf{OR}^7; -\mathsf{NR}^7 \mathsf{R}^8; -\mathsf{SR}^7; -\mathsf{S}(\mathsf{O}) \mathsf{R}^7; -\mathsf{SO}_2 \mathsf{R}^7; -\mathsf{SO}_3 \mathsf{R}^7; -\mathsf{CO}_2 \mathsf{R}^7; -\mathsf{SO}_3 \mathsf{R}^7$ heterocyclylalkyl, and polyether substituents of the RY radicals optionally wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, CONR 7R 8; -N+R 7R 8R 9A.; -P(O)R 7R 8; -PR 7R 8; -P+R 7R 8R 9A; and alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quatemary

may have one or more carbons replaced by -O-; -NR<sup>7</sup>-; -N<sup>+</sup>R<sup>7</sup>R<sup>8</sup>A--; -S-; heterocyclylalkyl, and polyether substituents of the  $\mathbb{R}^{\mathcal{Y}}$  radicals optionally SO-; -SO2-; -S<sup>+</sup>R<sup>7</sup>A-; -PR<sup>7</sup>-; -P(O)R<sup>7</sup>-; -P<sup>+</sup>R<sup>7</sup>R<sup>8</sup>A-; or phenylene; and wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl,

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P(O)(OR7)OR8; and

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alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and wherein R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> are independently selected from the alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; wherein R<sup>7</sup> and R<sup>8</sup> are independently selected from the group group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl;

wherein R13 and R14 together with the nitrogen atom to which they substituted with one or more radicals selected from the group consisting of are attached form a mono- or polycyclic heterocyclyl that is optionally oxo, carboxy, and quaternary salts; or

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wherein  $R^{14}$  and  $R^{15}$  together with the nitrogen atom to which they

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are attached form a cyclic ring; and

arylalkyl; heterocyciylalkyl; quatemary heterocyciylalkyl; alkylarylalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; wherein the R 13, R 14, and R 15 alkyl; haloalkyl; cycloalkyl;

- ukylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected nydroxyalkyi; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl;
- guanidinyl; -OR<sup>16</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>W</sup>A<sup>-</sup>; -SR<sup>16</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>;  $PR^9R^{10}; -P^+R^9R^{10}R^{11}A_-; -S^+R^9R^{10}A_+;$  and carbohydrate residue; and wherein the  $R^{13}, R^{14}, {\rm and}\ R^{15}\, {\rm alkyl};$  haloalkyl; cycloalkyl; heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; 2
  - ulkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O.; -NR9-; arylalkyi; heterocyclylalkyi; quatemary heterocyclylalkyi; alkylarylalkyi; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quatemary heterocyclyl; ulkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; 2
- N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A:; -S.; -SO.; -SO<sub>2</sub>; -S<sup>+</sup>R<sup>9</sup>A:; -PR<sup>9</sup>:; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A:; -P(O)R<sup>9</sup>.; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and 2

wherein R<sup>16</sup> and R<sup>17</sup> are independently selected from the group consisting of R9 and M; and

wherein R, R', R', R', R', and A are as previously set forth above wherein M is a pharmaceutically acceptable cation; and for the compounds of Formula I. 23

Still more preferably, at least one of R3 or R6 has the formula (II)

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wherein R' and t are defined as above.

In the various embodiments of the invention, the compounds of Formula I preferably satisfy at least one or more of the following additional conditions:

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 R¹ and R² are independently selected from the group consisting of hydrogen, alkyl and (C<sub>2-10</sub>)cycloalkyl. Preferably, R¹ and R² are

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independently selected from the group consisting of hydrogen and  $(C_1, \omega)$ alkyl. More preferably,  $R^1$  and  $R^2$  are independently selected from the group consisting of  $(C_{1,10})$ alkyl. Still more preferably,  $R^1$  and  $R^2$  are independently selected from the group consisting of  $(C_{1,2})$ alkyl. Still more preferably,  $R^1$  and  $R^2$  are independently selected from the group consisting of  $(C_{2,2})$ alkyl. Still more preferably,  $R^1$  and  $R^2$  are the same  $(C_{2,2})$ alkyl. Still more preferably,  $R^1$  and  $R^2$  are each n-butyl; and/or

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- (2) R<sup>3</sup> and R<sup>4</sup> are independently selected from the group consisting of hydrogen and -OR<sup>9</sup> wherein R<sup>9</sup> is defined as previously set forth above for the compounds of Formula I. Preferably, R<sup>3</sup> is hydrogen and R<sup>4</sup> is -OR<sup>9</sup>.
- Still more preferably, R<sup>3</sup> is hydrogen and R<sup>4</sup> is hydroxy. Still more preferably, the hydroxy group is in a syn relationship to the structure of Formula II; and/or

20

(3) R<sup>5</sup> is phenyl substituted with a radical selected from the group

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consisting of -OR<sup>13</sup>, -NR<sup>13</sup>C(O)R<sup>14</sup>, -NR<sup>13</sup>C(O)NR<sup>14</sup>R<sup>13</sup>, -NR<sup>13</sup>CO<sub>2</sub>R<sup>14</sup>, -OC(O)R<sup>13</sup>, -OC(O)NR<sup>13</sup>R<sup>14</sup>, -NR<sup>13</sup>SOR<sup>14</sup>, -NR<sup>13</sup>SO<sub>2</sub>R<sup>14</sup>, -NR<sup>13</sup>SONR<sup>14</sup>R<sup>13</sup>, and -NR<sup>13</sup>SO<sub>2</sub>NR<sup>14</sup>R<sup>13</sup> wherein R<sup>13</sup>, R<sup>14</sup> and R<sup>13</sup> are as previously set forth above for the compounds of Formula I. Still more preferably, R<sup>5</sup> is phenyl substituted with -OR<sup>13</sup> or -NR<sup>13</sup>C(O)R<sup>14</sup>. Still more preferably, R<sup>5</sup> is phenyl substituted at the para or meta position with -OR<sup>13</sup> wherein R<sup>13</sup> comprises a quaternary heterocyclyl, quaternary heterocyclylalkyl or alkylammoniumalkyl, or R<sup>5</sup> is phenyl substituted at the para or meta position with -NR<sup>13</sup>C(O)R<sup>14</sup> wherein R<sup>13</sup> is hydrogen and R<sup>14</sup> comprises a quaternary heterocyclyl, quaternary heterocyclylalkyl or

(4) R6 is hydrogen; and/or

alkylammoniumalkyl; and/or

- (5) R<sup>N</sup> is selected from the group consisting of hydrogen, alkyl and aralkyl. Preferably, R<sup>N</sup> is selected from the group consisting of hydrogen,
  15 (C<sub>1-10</sub>)alkyl and aryl(C<sub>1-10</sub>)alkyl. More preferably, R<sup>N</sup> is selected from the group consisting of hydrogen, methyl, ethyl and benzyl. Still more preferably, R<sup>N</sup> is hydrogen; and/or
- (6) R\* is independently selected from the group consisting of -OR<sup>13</sup>, NR<sup>13</sup>R', -N'R<sup>13</sup>R', and polyether. More preferably, R\* is selected from the group consisting of -OR<sup>13</sup> and -NR<sup>13</sup>R'. Still more preferably, R\* is selected from the group consisting of alkoxy, amino, alkylamino and dialkylamino. Still more preferably, R\* is selected from the group consisting of methoxy and dimethylamino; and/or
- (7) One or more R\* are present at the 7-, 8- or 9-position of the benzo
  25 ring of the structure of Formula I. Preferably, said R\* are present at the 7and 9-positions of the benzo ring of the structure of Formula I. More
  preferably, R\* is present at the 7-position of the benzo ring of the structure of
  Formula I; and/or
- (8) q is 1, 2 or 3. Preferably, q is 1 or 2, and more preferably q is 1;

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and/or

(9) t is 1 or 2.

Formula I satisfy at least one or more of the above-described conditions and In still another embodiment of the invention, the compounds of R3 comprises a carbohydrate residue. A more preferred class of compounds comprises those compounds of Formula I wherein:

q is an integer from 1 to 4;

R1 and R2 are independently selected from the group consisting of

hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; arylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; alkylaryl; and (polyalkyl)aryl; or 2

 $R^{\mbox{\scriptsize 1}}$  and  $R^{\mbox{\scriptsize 2}}$  taken together with the carbon to which they are attached form C<sub>3</sub>-C<sub>10</sub> cycloalkyl or C<sub>3</sub>-C<sub>10</sub> cycloalkenyl; and

- wherein the R 1 and R2 alkyl; cycloalkyl; alkenyl; alkynyl; arylalkyl; N\*R<sup>9</sup>R<sup>10</sup>R<sup>W</sup>A; -SR<sup>9</sup>; -S\*RR<sup>10</sup>A; -PR<sup>9</sup>R<sup>10</sup>; -P\*R<sup>9</sup>R<sup>10</sup>RWA; -S(O)R<sup>9</sup>; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may be substituted with one or more radicals selected from the group consisting of -CN; halogen; oxo; -0R  $^9;$  -NR  $^9R \, ^{10};$  -SO2R<sup>9</sup>; -SO3R<sup>9</sup>; -CO2R<sup>9</sup>; and -CONR<sup>9</sup>R<sup>10</sup>; and 2
- wherein the R 1 and R 2 alkyl; cycloalkyl; alkenyl; alkynyl; arylalkyl; radicals optionally may have one or more carbons replaced by -O.; -NR 9.; -N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A<sup>-</sup>; -S-; -SO-; -SO<sub>2</sub>; -S<sup>+</sup>R<sup>9</sup>A<sup>-</sup>-; -PR<sup>9</sup>-; -P(O)R<sup>9</sup>-; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A<sup>-</sup>-; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; alkylaryl; and (polyalkyl)aryl or phenylene; and ន
- wherein  $\mathbb{R}^9$  ,  $\mathbb{R}^{10}$  , and  $\mathbb{R}^w$  are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl; 23

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carboxyalkyl; carboalkoxyalkyl; carboxyheterocyclyl; carboxyalkylamino;

wherein A is a pharmaceutically acceptable anion; and

 $\mathbb{R}^3$  and  $\mathbb{R}^4$  are independently selected from the group consisting of

R<sup>3</sup> and R<sup>4</sup> together form =0; =NOR<sup>9</sup>; =S; =NNR<sup>9</sup>R<sup>10</sup>; =NR<sup>9</sup>; or hydrogen; alkyi; alkenyi; alkynyl; aryi; heterocyclyi; -OR<sup>9</sup>; -NR<sup>9</sup>R <sup>10</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; and -SO<sub>3</sub>R<sup>9</sup>; or

cyanoalkyi; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>9</sup>; -CO<sub>2</sub>R<sup>9</sup>; consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkynyl; aryl; wherein R<sup>11</sup> and R<sup>12</sup> are independently selected from the group heterocyclyl; arylalkyl; carboxyalkyl; carboalkoxyalkyl; cycloalkyl; and -CONR9R10; or 2

 $R^{11} \ \mathrm{and} \ R^{12}$  together with the carbon atom to which they are

attached form a cyclic ring; and 12

wherein R9 and R10 are as defined above; and

hydrogen; alkyi; cycloalkyi; alkenyi; alkynyi; aryi; heterocyclyi; quatemary  $m R^5$  and  $m R^6$  are independently selected from the group consisting of heterocyclyl;  $-OR^9$ ;  $-SR^9$ ;  $-S(O)R^9$ ;  $-SO_2R^9$ ; and  $-SO_3R^9$ ;

- substituted with one or more radicals independently selected from the group cycloalkyi; alkenyi; alkynyl; aryi; heterocyclyl; quaternary heterocyclyl; wherein the  $R^5$  and  $R^6$  alkyl; cycloalkyl; alkenyl; aryl; aryl; heterocyclyl; and quaternary heterocyclyl radicals optionally may be consisting of halogen; -CN; -NO2; oxo; alkyl; polyalkyl; haloalkyl; 2
  - 5(0)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO<sub>2</sub>R<sup>13</sup>; - $0M; -SO_2OM; -SO_2NR^{13}R^{14}; -C(0)NR^{13}R^{14}; -C(0)OM; -COR^{13};$ arylalkyl; heterocyclylalkyl; polyether; -OR13; -NR13R14; -SR13; . JC(0)NR<sup>13</sup>R<sup>14</sup>; -NR<sup>13</sup>SOR<sup>14</sup>; -NR<sup>13</sup>SO<sub>2</sub>R<sup>14</sup>; -NR<sup>13</sup>SONR<sup>14</sup>R<sup>15</sup>; NR13C(O)R14; -NR13C(O)NR14R15; -NR13CO3R14; -OC(O)R13; 52

P(OR<sup>13</sup>)OR<sup>14</sup>; -S<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A<sup>-</sup>; and -N<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>-</sup>; and NR"SO,NR"R"; -PR<sup>13</sup>R<sup>14</sup>; -P(O)R<sup>13</sup>R<sup>14</sup>; -P<sup>†</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>\*</sup>; -

5 CONR 7 8; -N+R 7 R 8 R 9 A-; -P(O)R 7 R 8; -PR 7 R 8; -P+R 7 R 8 R 9 A; and -P(O)(OR')OR'; and alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl, and polyether substituents of the R' and R' radicals heterocyclyl; -OR<sup>7</sup>; -NR<sup>7</sup>R<sup>8</sup>; -SR<sup>7</sup>; -S(O)R<sup>7</sup>; -SO<sub>2</sub>R<sup>7</sup>; -SO<sub>3</sub>R<sup>7</sup>; -CO<sub>2</sub>R<sup>7</sup>; from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; optionally may be further substituted with one or more radicals selected alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl,

heterocyclylalkyl, and polyether substituents of the R' and R' radicals alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl

 $N^{+}R^{7}R^{8}A: -S: -SO: -SO: -SO: -S^{+}R^{7}A: -PR^{7}: -P(O)R^{7}: -P^{+}R^{7}R^{8}A: -or$ optionally may have one or more carbons replaced by -O-; -NR  $^\prime$ -; phenylene; and

5

consisting of hydrogen and alkyl; and wherein  $R^7$  and  $R^8$  are independently selected from the group

20 alkylheterocyclylalkyl; alkylammoniumalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; wherein  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  are independently selected from the

23 carboxyalkylaminocarbonylalkyl; and polyether; or

are attached form a mono- or polycyclic heterocyclyl that is optionally oxo, carboxy, and quaternary salts; or substituted with one or more radicals selected from the group consisting of wherein R13 and R14 together with the nitrogen atom to which they

are attached form a cyclic ring; and wherein  $\mathbb{R}^{14}$  and  $\mathbb{R}^{15}$  together with the nitrogen atom to which they

5 heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; from the group consisting of halogen; -CN; sulfo; oxo; alkyl; sulfoalkyl; radicals optionally may be substituted with one or more radicals selected wherein the  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  alkyl; haloalkyl; cycloalkyl;

2 polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; and carbohydrate residue; and wherein the R  $^{13}$ , R  $^{14}$ , and R  $^{15}$  alkyl; haloalkyl; cycloalkyl;

SR<sup>16</sup>; -S(0)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>16</sup>; -CO<sub>2</sub>R<sup>16</sup>; -CONR<sup>9</sup>R<sup>10</sup>; -

carboxy; carboxyalkyl; guanidinyl; -OR $^{16}$ , -NR $^{9}$ R $^{10}$ , -N $^{+}$ R $^{9}$ R $^{10}$ R $^{w}$ A $^{-}$ ; -

SO2NR9R10; -PO(OR16)OR17; -PR9R10; -P+R9R10R11A; -S+R9R10A

alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl;

8 polypeptide residue; and phenylene; carbohydrate residue; amino acid residue; peptide residue; or N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A·; -S·; -SO·; -SO<sub>2</sub>; -S<sup>+</sup>R<sup>9</sup>A·; -PR<sup>9</sup>·; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A·; -P(0)R<sup>9</sup>radicals optionally may have one or more carbons replaced by -O-; -NR<sup>9</sup>-;

25 consisting of R<sup>9</sup> and M; and wherein  $\mathbb{R}^{16}$  and  $\mathbb{R}^{17}$  are independently selected from the group

alkynyi; and aralkyi; and  $\mathbb{R}^N$  is selected from the group consisting of hydrogen; alkyl; alkenyl; wherein M is a pharmaceutically acceptable cation; and wherein R?, R10, R11, R12, Rw, and A are as defined above; and

one or more R<sup>x</sup> radicals are independently selected from the group consisting of hydrogen; halogen; -CN; -NO2; alkyl; cycloalkyl; polyalkyl; haloalkyl; alknyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; polyether; acyloxy; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -S<sup>2</sup>R<sup>13</sup>R<sup>14</sup>A; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO<sub>2</sub>R<sup>13</sup>; -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>; -NR<sup>13</sup>CO)R<sup>13</sup>; -CO)Ni; -COON; -COR<sup>13</sup>; -OR<sup>13</sup>; -S(O)<sub>I</sub>NR<sup>13</sup>R<sup>14</sup>; -NR<sup>13</sup>R<sup>14</sup>; -NR<sup>13</sup>R<sup>14</sup>; -NR<sup>13</sup>R<sup>14</sup>; -P<sup>1</sup>R<sup>13</sup>R<sup>14</sup>; -P<sup>1</sup>R<sup>13</sup>R<sup>14</sup>; -P<sup>1</sup>R<sup>13</sup>R<sup>14</sup>; -P<sup>1</sup>R<sup>13</sup>R<sup>14</sup>; amino acid residue; peptide acid residue; polypeptide acid residue; and carbohydrate acid residue;

wherein the R' alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy radicals optionally may be further substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; -OR<sup>16</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N<sup>2</sup>R<sup>9</sup>R<sup>10</sup>; -SO<sub>2</sub>NR<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>16</sup>; -CO<sub>2</sub>R<sup>16</sup>; -CO<sub>2</sub>R<sup>16</sup>; -CO<sub>2</sub>R<sup>16</sup>; -CO<sub>3</sub>R<sup>16</sup>; -CO<sub>3</sub>R<sup>16</sup>; -A<sup>2</sup>R<sup>10</sup>; -PO(OR<sup>16</sup>)OR<sup>17</sup>; -PR<sup>9</sup>R<sup>10</sup>; -PR<sup>9</sup>R<sup>10</sup>; -PR<sup>9</sup>R<sup>10</sup>; -PR<sup>9</sup>R<sup>10</sup>; -Rad carbohydrate acid residue; and

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wherein the R\* quaternary heterocyclyl radical optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; -NO2; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; polyether; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -NR<sup>13</sup>CR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -C(O)OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>OM; -COONR<sup>13</sup>R<sup>14</sup>; -C(O)OM; -COR<sup>13</sup>; -R(O)R<sup>13</sup>R<sup>14</sup>; -P<sup>1</sup>R<sup>13</sup>R<sup>14</sup>; -P<sup>1</sup>R<sup>13</sup>R<sup>14</sup>; -P(O)OM; -COR<sup>13</sup>; -S<sup>14</sup>R<sup>13</sup>R<sup>14</sup>; -P<sup>1</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>1</sup>; -P(OR<sup>13</sup>)OR<sup>14</sup>; -S<sup>14</sup>R<sup>13</sup>R<sup>14</sup>A<sup>1</sup>; -N<sup>14</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>1</sup>; and carbohydrate acid residue; and

wherein the R<sup>x</sup> radicals comprising carbon optionally may have one or more carbons replaced by -O.; -NR<sup>13</sup>; -N<sup>\*</sup>R<sup>13</sup>R<sup>14</sup>A·; -S.; -SO.; -SO<sub>2</sub>; -S<sup>\*</sup>R<sup>13</sup>A<sup>\*</sup>.; -PR<sup>13</sup>, -PR<sup>13</sup>; -PR<sup>13</sup>R<sup>14</sup>A·; phenylene; amino

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acid, peptide; polypeptide; carbohydrate; polyether; or polyalkyl; wherein said phenylene; amino acid; peptide; polypeptide; carbohydrate; and polyalkyl optionally may have one or more carbons replaced by -O-; -NR  $^9$ -; -N^+R $^9$ R $^1$ OA-; -S-; -SO-; -SO<sub>2</sub>-; -S^+R $^9$ -; -PR $^9$ -; -P $^+$ R $^9$ R $^1$ OA-; or -

5 P(O)R%-; and

wherein R<sup>18</sup> is selected from the group consisting of alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and

wherein the R<sup>18</sup> alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quatemary heterocyclyl; arylalkyl; heterocyclylalkoxycarbonyl; arylalkoxycarbonyl; arylalkoxycarbonyl; arylalkoxycarbonyl; arylalkoxycarbonyl radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N<sup>+</sup>R<sup>9</sup>R<sup>11</sup>R<sup>12</sup>A<sup>-</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -CONR<sup>9</sup>R<sup>10</sup>; -SO<sub>2</sub>OM; -SO<sub>2</sub>NR<sup>9</sup>; -PR<sup>9</sup>R<sup>10</sup>; -PR<sup>10</sup>; -PR<sup>1</sup>

wherein R, Rio, RII, RI3, RI4, RI3, RI6, RI7, RW, AT, and M are as defined above; or

20 a pharmaceutically acceptable salt, solvate, or prodrug thereof.

A class of compounds of interest comprises those compounds of Formula I wherein:

q is an integer from 1 to 4;

 $R^1$  and  $R^2$  are independently selected from the group consisting of hydrogen;  $(C_1\text{-}C_{10})alkyl; \, (C_2\text{-}C_{10})alkyl; \, (C_2\text{-}C_{10})alkenyl; \, (C_2\text{-}C_{10})a$ 

25 hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>2</sub>-C<sub>10</sub>)cycloalkyl; (C<sub>2</sub>-C<sub>10</sub>)alkenyl; (C<sub>2</sub>-C<sub>10</sub>)alkynyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>2</sub>-C<sub>10</sub>)alkylyl; (C<sub>1</sub>-C<sub>10</sub>)alkylylylyly; and (polyalkyl)aryl; or

PTRYR10RWA; -S(0)R9; -SO2R9; -SO3R9; -CO2R9; and -CONR9R10; oxo; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>W</sup>A<sup>\*</sup>; -SR<sup>9</sup>; -S<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A<sup>\*</sup>; -PR<sup>9</sup>R<sup>10</sup>; one or more radicals selected from the group consisting of -CN; halogen; C10) alkylaryl; and (polyalkyl) aryl radicals optionally may be substituted with  $(C_1-C_{10})$ alkoxy $(C_7-C_{10})$ alkenyl;  $(C_1-C_{10})$ alkoxy $(C_7-C_{10})$ alkynyl;  $(C_1-C_{10})$ alkoxy  $C_{10}$ )alkenyl;  $(C_2-C_{10})$ alkynyl; aryl $(C_1-C_{10})$ alkyl;  $(C_1-C_{10})$ alkoxy $(C_1-C_{10})$ alkyl; wherein the  $\mathbb{R}^1$  and  $\mathbb{R}^2$  (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl; (C<sub>2</sub>

carbons replaced by -O-; -NR<sup>9</sup>-; -N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A<sup>-</sup>-; -S-; -SO-; -SO<sub>2</sub>-; -S<sup>+</sup>R<sup>9</sup>A<sup>-</sup>-; -PR $^9$ ; -P(O)R $^9$ -; -P $^+$ R $^9$ R $^{10}$ A $^-$ -; or phenylene; and  $C_{10}$ )alkylaryl; and (polyalkyl)aryl radicals optionally may have one or more  $(C_1-C_{10})$ alkoxy $(C_2-C_{10})$ alkenyl;  $(C_1-C_{10})$ alkoxy $(C_2-C_{10})$ alkynyl;  $(C_1-C_{10})$ alkoxy  $C_{10}$ )alkenyl;  $(C_2-C_{10})$ alkynyl; aryl $(C_1-C_{10})$ alkyl;  $(C_1-C_{10})$ alkoxy $(C_1-C_{10})$ alkyl; wherein the  $\mathbb{R}^1$  and  $\mathbb{R}^2$  (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl; (C<sub>3</sub>-

C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>2</sub>-C<sub>10</sub>)cycloalkyl; (C<sub>2</sub>-C<sub>10</sub>)alkenyl; (C<sub>2</sub>-C<sub>10</sub>)alkynyl; aryl; heterocyclyl; ammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>wherein  $\mathbb{R}^9$ ,  $\mathbb{R}^{10}$ , and  $\mathbb{R}^w$  are independently selected from the group

20 carboxyheterocyclyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkylamino; and acyl; and C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; carbo(C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>1</sub>-C<sub>10</sub>)alkyl;  $\mathbb{R}^3$  and  $\mathbb{R}^4$  are independently selected from the group consisting of wherein A is a pharmaceutically acceptable anion; and

hydrogen;  $(C_1-C_{10})$ alkyl;  $(C_2-C_{10})$ alkenyl;  $(C_2-C_{10})$ alkynyl; aryl; heterocyclyl;  $-OR^9$ ;  $-NR^9R^{10}$ ;  $-SR^9$ ;  $-S(O)R^9$ ;  $-SO_2R^9$ ; and  $-SO_3R^9$ ; or R<sup>3</sup> and R<sup>4</sup> together form =O; =NOR<sup>9</sup>; =S; =NNR<sup>9</sup>R<sup>10</sup>; =NR<sup>9</sup>; or

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wherein  $\mathbb{R}^{11}$  and  $\mathbb{R}^{12}$  are independently selected from the group

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CONR9R10; or OR9; -NR9R10; -SR9; -S(O)R9; -SO2R9; -SO3R9; -CO2R9; and  $carbo(C_1\text{-}C_{10})alkoxy(C_1\text{-}C_{10})alkyl; \ (C_3\text{-}C_{10})cycloalkyl; \ cyano(C_1\text{-}C_{10})alkyl; \ \cdot$ (C<sub>2</sub>-C<sub>10</sub>)alkynyl; aryl; heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; consisting of hydrogen; -CN; halogen; oxo; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>2</sub>-C<sub>10</sub>)alkenyl;

attached form a cyclic ring; and  $\mathbb{R}^{11}$  and  $\mathbb{R}^{12}$  together with the carbon atom to which they are

wherein R<sup>9</sup> and R <sup>10</sup> are as defined above; and

hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>2</sub>-C<sub>10</sub>)cycloalkyl; (C<sub>2</sub>-C<sub>10</sub>)alkenyl; (C<sub>2</sub>-S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; and -SO<sub>3</sub>R<sup>9</sup>; C<sub>10</sub>)alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; -OR<sup>9</sup>; -SR<sup>9</sup>; - $\mathbb{R}^5$  and  $\mathbb{R}^6$  are independently selected from the group consisting of

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ᅜ -SR<sup>13</sup>; -S(0)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; radicals optionally may be substituted with one or more radicals aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; polyether; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>, C<sub>10</sub>)alkenyl; (C<sub>2</sub>-C<sub>10</sub>)alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; oxo;  $(C_1-C_{10})$ alkyl; polyalkyl; halo $(C_1-C_{10})$ alkyl;  $(C_3-C_{10})$ cycloalkyl;  $(C_2-C_{10})$ independently selected from the group consisting of halogen; -CN; -NO2;  $C_{10}$ ) alkenyl;  $(C_7-C_{10})$  alkynyl; aryl; heterocyclyl; and quaternary heterocyclyl wherein the  $R^5$  and  $R^6$  (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>2</sub>-C<sub>10</sub>)cycloalkyl; (C<sub>2</sub>-

25 P(OR 13)OR 14; -S+R 13R 14A; and -N+R 13R 14R 15A; and COR 13; -NR 13C(O)R 14; -NR 13C(O)NR 14R 11; -NR 13CO,R 14; -OC(O)R 13; - $CO_2R^{13}$ ; -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>; -C(O)NR<sup>13</sup>R<sup>14</sup>; -C(O)OM; OC(O)NR'3R'4; -NR'3SOR'4; -NR'3SO,R'4; -NR'3SONR'4R'5; -NR''3O,NR''R''; -P(O)R<sup>13</sup>R<sup>14</sup>; -PR<sup>13</sup>R<sup>14</sup>; -P<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>-</sup>; -

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C10) alkyl, and polyether substituents of the R2 and R6 radicals optionally C<sub>10</sub>)alkyl, (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl, (C<sub>2</sub>-C<sub>10</sub>)alkenyl, (C<sub>7</sub>-C<sub>10</sub>)alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, aryl( $C_i$ - $C_{i0}$ )alkyl, heterocyclyl( $C_i$ wherein the (C<sub>1</sub>-C<sub>10</sub>)alkyl, polyalkyl, halo(C<sub>1</sub>-C<sub>10</sub>)alkyl, hydroxy(C<sub>1</sub>-

may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary heterocyclyl; -OR<sup>7</sup>; -NR<sup>7</sup>R<sup>8</sup>; -SR<sup>7</sup>; -(C2-C10)alkenyl; (C2-C10)alkynyl; aryl; heterocyclyl; aryl(C1-C10)alkyl;  $S(O)R^7$ ;  $-SO_2R^7$ ;  $-SO_3R^7$ ;  $-CO_2R^7$ ;  $-CONR^7R^8$ ;  $-N^4R^7R^8R^9A_2$ ; - $P(O)R^7R^8; \ -PR^7R^8; \ -P^+R^7R^8R^9A^7; \ and \ -P(O)(OR^7)OR^8; \ and$ 

wherein the (C1-C10)alkyl, polyalkyl, halo(C1-C10)alkyl, hydroxy(C1may have one or more carbons replaced by -O-; -NR  $^7$ ; -N $^+$ R  $^7$ R  $^8$ A--; -S-; SO.; .SO2.;  $.S^{+}R^{7}A.$ ;  $.PR^{-}$ ;  $.P(O)R^{7}$ ;  $.P^{+}R^{7}R^{8}A.$ ; or phenylene; and heterocyclyl, quaternary heterocyclyl, aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl, heterocyclyl(C<sub>1</sub>-C10, alkyl, and polyether substituents of the R3 and R6 radicals optionally wherein  $\boldsymbol{R}^{\boldsymbol{A}}$  and  $\boldsymbol{R}^{\boldsymbol{8}}$  are independently selected from the group C<sub>10</sub>)alkyl, (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl, (C<sub>2</sub>-C<sub>10</sub>)alkenyl, (C<sub>3</sub>-C<sub>10</sub>)alkynyl, aryl, consisting of hydrogen and (C1-C10)alkyl; and 2

heterocyclyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>wherein  $R^{13},\,R^{14},\,$  and  $R^{15}$  are independently selected from the C10, alkyl; quaternary heterocyclyl(C1-C10, alkyl; (C1-C10, alkylaryl(C1group consisting of hydrogen; (C<sub>I</sub>-C<sub>10</sub>)alkyl; halo(C<sub>I</sub>-C<sub>10</sub>)alkyl; (C<sub>I</sub>-C10)cycloalkyl; polyalkyl; (C2-C10)alkenyl; (C2-C10)alkynyl; aryl; C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylheterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-2 2

wherein R13 and R14 together with the nitrogen atom to which they C10)alkyl; and polyether; or

 $C_{10}$ ) alky lammonium ( $C_1$ - $C_{10}$ ) alky  $I_2$ ; carboxy ( $C_1$ - $C_{10}$ ) alky lamino carbony  $I(C_1$ -

substituted with one or more radicals selected from the group consisting of are attached form a mono- or polycyclic heterocyclyl that is optionally oxo, carboxy, and quaternary salts; or

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wherein  $\mathbb{R}^{14}$  and  $\mathbb{R}^{15}$  together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the  $\rm R^{13}$ ,  $\rm R^{14}$ , and  $\rm R^{15}$  (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-

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heterocyclyl; quaternary heterocyclyl; aryl(C1-C10)alkyl; heterocyclyl(C1-C<sub>10</sub>)alkyi; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyi; (C<sub>1</sub>-C<sub>10</sub>)alkylaryl (C<sub>1</sub>-Cio)cycloalkyl; polyalkyl; (C<sub>2</sub>-C<sub>10</sub>)alkenyl; (C<sub>2</sub>-C<sub>10</sub>)alkynyl; aryl; C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylheterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-

- oxo; (C<sub>1</sub>-C<sub>10</sub>)alkyl; sulfo(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary heterocyclyl; (C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; C<sub>10</sub>)alkylaminocarbonyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkylaminocarbonyl C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; aminocarbonyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-
- wherein the R 13, R 14, and R 15 (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>guanidinyl; -OR 16; -NR 9R 10; -N\*R 9R 10R WA; -SR 16; -S(O)R 9; -SO2R 9; PR9R10; -P+R9R10R11A-;-S+R9R10A-; and carbohydrate residue; and  $- \cos^{16} : -\cos^{16} : -\cos^{9} \sin^{9} : - \cos^{10} : -\cos^{10} : -\cos^{10} : \cos^{10} : \cos^{10}$ quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; 2
- heterocyclyt; quaternary heterocyclyt; aryt(C<sub>1</sub>-C<sub>10</sub>)alkyt; heterocyclyt(C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylaryl(C<sub>1</sub>-C<sub>10</sub>)cycloalkyl; polyalkyl; (C<sub>2</sub>-C<sub>10</sub>)alkenyl; (C<sub>2</sub>-C<sub>10</sub>)alkynyl; aryl; C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylheterocyclyi(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-13
  - C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; aminocarbonyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylaminocarbonyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-ನ
- C10, alkylaminocarbonyl (C1-C10, alkyl; and polyether radicals optionally may have one or more carbons replaced by -O.; -NRP.; -NTRPR 10A.; -S.; -SO.;  $\cdot SO_2 \cdot \cdot \cdot \cdot S^+R^9A \cdot \cdot \cdot \cdot \cdot P^+R^9R^{10}A \cdot \cdot \cdot \cdot P(0)R^9 \cdot \cdot \text{ phenylene; carbohydrate}$ residue; amino acid residue; peptide residue; or polypeptide residue; and
  - wherein  $R^{\mbox{\scriptsize 16}}$  and  $R^{\mbox{\scriptsize 17}}$  are independently selected from the group consisting of R9 and M; and 23

 $R^{\mathbf{N}}$  is selected from the group consisting of hydrogen; (C<sub>I</sub>-C<sub>I0</sub>)alkyl; wherein R, R10, R11, R12, R, and A are as defined above; and wherein M is a pharmaceutically acceptable cation; and

 $(C_2-C_{10})$ alkenyl;  $(C_2-C_{10})$ alkynyl; and aryl $(C_1-C_{10})$ alkyl; and

 $C_{10}$ )cycloalkyl; polyalkyl; halo $(C_1-C_{10})$ alkyl;  $(C_2-C_{10})$ alkenyl;  $(C_3-C_{10})$ consisting of hydrogen; halogen; -CN; -NO2; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>one or more RX radicals are independently selected from the group

- $SO_2OM; -SO_2NR^{13}R^{14}; -NR''C(O)R''; -C(O)NR^{12}R^{14}; -C(O)OM;$ polyether; acyloxy; -OR  $^{13}$ ; -NR  $^{13}$ R  $^{14}$ ; -SR  $^{13}$ ; -S(O)R  $^$ C10)alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; aryl(C1-C10)alkyl; COR<sup>13</sup>; -OR<sup>18</sup>; -S(O)<sub>n</sub>NR<sup>13</sup>R<sup>14</sup>; -NR<sup>13</sup>R<sup>18</sup>; -NR<sup>18</sup>OR<sup>14</sup>; -SO3R<sup>13</sup>; -S<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO2R<sup>13</sup>; -OM;
- 5 acid residue; peptide acid residue; polypeptide acid residue; and N<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>-</sup>; -PR<sup>13</sup>R<sup>14</sup>; -P(O)R<sup>13</sup>R<sup>14</sup>; -P<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>-</sup>; amino carbohydrate acid residue;

SO3R 16; -CO2R 16; -CONR 9R 10; -SO2NR 9R 10; -PO(OR 15)OR 17; oxo;  $-OR^{16}$ ;  $-NR^{9}R^{10}$ ;  $-N^{+}R^{9}R^{11}R^{12}A^{-}$ ;  $-SR^{16}$ ;  $-S(O)R^{9}$ ;  $-SO_{2}R^{9}$ ; acyloxy radicals optionally may be further substituted with halogen; -CN; heterocyclyl;  $aryl(C_1-C_{10})alkyl$ ; heterocyclyl $(C_1-C_{10})alkyl$ ; polyether;  $C_{10}$ )alkyl; hydroxy( $C_1$ - $C_{10}$ )alkyl; ( $C_2$ - $C_{10}$ )alkenyl; ( $C_2$ - $C_{10}$ )alkynyl; aryl; wherein the  $R^*$  ( $C_i$ - $C_{10}$ )alkyl; ( $C_j$ - $C_{10}$ )cycloalkyl; polyalkyl; halo( $C_i$ 

 $PR^{9}R^{10}$ ;  $.P^{+}R^{9}R^{11}R^{12}A^{-}$ ; or  $.S^{+}R^{9}R^{10}A^{-}$ ; and

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ટ્ડ 20 OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; P+R13R14R15A;-P(OR13)OR14;-S+R13R14A; and N+R13R14R15A; C(0)NR<sup>13</sup>R<sup>14</sup>; -C(0)OM; -COR<sup>13</sup>; -P(0)R<sup>13</sup>R<sup>14</sup>; -PR<sup>13</sup>R<sup>14</sup>;  $NR^{13}NR^{14}R^{15}$ ; -CO2R<sup>13</sup>; -OM; -SO2OM; -SO2NR<sup>13</sup>R<sup>14</sup>; aryl; heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; polyether;  $halo(C_1-C_{10})alkyl;\ hydroxy(C_1-C_{10})alkyl;\ (C_2-C_{10})alkenyl;\ (C_3-C_{10})alkynyl;$ halogen; -CN; -NO2; oxo; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl; polyalkyl; substituted with one or more radicals selected from the group consisting of wherein the R\* quaternary heterocyclyl radical optionally may be

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-S<sup>+</sup>R<sup>13</sup>A<sup>-</sup>; -PR<sup>13</sup>-; -P(O)R<sup>13</sup>-; -PR<sup>13</sup>-; -P<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A<sup>-</sup>; phenylene; amino or more carbons replaced by -O-; -NR $^{13}$ -; -N $^+$ R $^{13}$ R $^{14}$ A-; -S-; -SO-; -SO<sub>2</sub>-; acid residue; peptide residue; polypeptide residue; carbohydrate residue; wherein the Rx radicals comprising carbon optionally may have one

SO-; -SO<sub>2</sub>-; -S<sup>+</sup>R<sup>9</sup>A-; -PR<sup>9</sup>-; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-; or -P(O)R<sup>9</sup>-; and may have one or more carbons replaced by -O-; -NR $^9$ -; -N $^+$ R $^9$ R $^{10}$ A $^-$ -; -S-; polyether; or polyalkyl; wherein said phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; and polyalkyl optionally

C<sub>10</sub>)alkoxycarbonyl; and heterocyclyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; acyl; and aryl(C<sub>1</sub>wherein  $R^{18}$  is selected from the group consisting of  $(C_i-C_{i0})$  alkyl;

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2 SO<sub>2</sub>NR<sup>9</sup>R<sup>10</sup>;-PR<sup>9</sup>R<sup>10</sup>;-P(OR<sup>13</sup>)OR<sup>14</sup>;-PO(OR<sup>16</sup>)OR<sup>17</sup>; and -C(O)OM; consisting of halogen; -CN; oxo; -OR9; -NR9R10; -N+R9R11R12A-; -SR9;  $-S(O)R^{9}; -SO_{2}R^{9}; -SO_{3}R^{9}; -CO_{2}R^{9}; -CONR^{9}R^{10}; -SO_{2}OM;$ may be substituted with one or more radicals selected from the group aryl( $C_1$ - $C_{10}$ )alkyl; acyl; and aryl( $C_1$ - $C_{10}$ )alkoxycarbonyl radicals optionally wherein the R18 (C1-C10)alkyl; heterocyclyl; quaternary heterocyclyl;

defined above; or wherein R°, R10, R11, R12, R14, R15, R16, R17, R\*, A\*, and M are as

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substituted phenyl, biphenyl and naphthyl; and provided that aryl is selected from the group consisting of optionally a pharmaceutically acceptable salt, solvate, or prodrug thereof; and

group consisting of oxygen, nitrogen, sulfur and phosphorus. optionally substituted heterocyclyl comprising a 5 to 10 membered ring and comprising one or more ring atoms that are heteroatoms selected from the provided that heterocyclyl is selected from the group consisting of

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A class of compounds of particular interest comprises those

q is an integer from 1 to 4;

compounds of Formula I wherein:

 ${\rm R}^1$  and  ${\rm R}^2$  are independently selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl,

- teri-butyl, pentyl, hexyl, phenoxymethylene, phenoxyethylene, phenoxypropylene, pyridinyloxymethylene, pyridinyloxyethylene; methylpyridinyloxymethylene, methylpyridinyloxyethylene, pyrimidinyloxymethylene, and pyrimidinyloxyethylene; or
- $R^1\, {\rm and}\, R^2$  taken together with the carbon to which they are attached form cyclopropyl, cyclobutyl, cyclopentyl, or cyclobexyl; and

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 $\rm R^3$  and  $\rm R^4$  are independently selected from the group consisting of hydrogen, hydroxy, methyl, ethyl, phenyl, pyridinyl, amino, methylamino, dimethylamino, ethylamino and diethylamino; and

R<sup>5</sup> and R<sup>6</sup> are independently selected from the group consisting of

- hydrogen, phenyl, chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, hydroxyphenyl, methoxyphenyl, ethoxyphenyl, methoxy(chlorophenyl), methoxy(fluorophenyl), methoxy(fluorophenyl), ethoxy(chlorophenyl), ethoxy(chlorophenyl), ethoxy(chlorophenyl), ethoxy(iodophenyl), methoxy(iodophenyl), mitrophenyl, aminophenyl, methylaminophenyl,
  - 20 dimethylaminophenyl, ethylaminophenyl, diethylaminophenyl, trimethylammoniumphenyl, triethylammoniumphenyl, trimethylammoniummethylcarbonylaminophenyl, triethylammoniummethylcarbonylaminophenyl, triethylammoniummethylcarbonylaminophenyl, trimethylammoniumethylcarbonylaminophenyl,
- 25 triethylammoniumethylcarbonylaminophenyl, trimethylammoniumpropylcarbonylaminophenyl, triethylammoniumpropylcarbonylaminophenyl, trimethylammoniumbutylcarbonylaminophenyl, triethylammoniumbutylcarbonylaminophenyl, methylcarbonylaminophenyl

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chloromethylcarbonylaminophenyl, fluoromethylcarbonylaminophenyl, bromomethylcarbonylaminophenyl, iodomethylcarbonylaminophenyl, ethylcarbonylaminophenyl, chloroethylcarbonylaminophenyl, fluoroethylcarbonylaminophenyl, bromoethylcarbonylaminophenyl,

- iodoethylcarbonylaminophenyl, propylcarbonylaminophenyl, chloropropylcarbonylaminophenyl, fluoropropylcarbonylaminophenyl, bromopropylcarbonylaminophenyl, iodopropylcarbonylaminophenyl, butylcarbonylaminophenyl, chlorobutylcarbonylaminophenyl, fluorobutylcarbonylaminophenyl, bromobutylcarbonylaminophenyl,
- iodobutylcarbonylaminophenyl, 3,4-dioxymethylenephenyl, pyridinyl, methylpyridinyl, pyridinium, methylpyridinium, thienyl, chlorothienyl, fluorothienyl, bromothienyl, iodothienyl; methoxycarbonylphenyl, ethoxycarbonylphenyl, trimethylammoniumethoxyethoxyethoxyphenyl, triethylammoniumethoxyethoxyethoxyphenyl,
- 15 chloroethoxyethoxyphenyl, fluoroethoxyethoxyphenyl, bromoethoxyethoxyphenyl, iodoethoxyethoxyethoxyphenyl, pyridiniumethoxyethoxyphenyl, piperazinyloxymethoxyethoxyphenyl,
- methylpiperazinyloxymethoxyethoxyethoxyphenyl,
  dimethylpiperazinyloxymethoxyethoxyethoxyphenyl,
  piperidinyloxymethoxyethoxyphenyl,
  methylpiperidinyloxymethoxyethoxyphenyl, and
  dimethylpiperidinyloxymethoxyethoxyphenyl; and

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 $R^{N}$  is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, n-butyl, n-bextyl and benzyl; and

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one or more R<sup>x</sup> radicals are independently selected from the group consisting of hydroxy, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, sec-butyl, methoxy, ethoxy, n-propoxy, isopropoxy, methylithio, methylsulfonyl, ethylsulfinyl, ethylsulfonyl,

methylcarbonylamino, chloromethylcarbonylamino, carboxymethyl-amino, N,N-dimethyl-N-carboxymethyl-ammonium diethylamino, trimethylammonium, triethylammonium, N-methyl-Namino, hydroxyamino, methylamino, dimethylamino, ethylamino,

5 methyl-pyrrolidinium, piperazinyl, N-methylpiperazinyl, N,N'-dimethylmethyl-morpholinium, azetidinyl, N-methyl-azetidinium, pyrrolidine, Npiperazinium, piperidinyl, methylpiperidinyl, N-methyl-piperidinium, and benzyloxycarbonylamino, aminoimidocarbonylamino, morpholinyl, Nbutylcarbonylamino, n-pentylcarbonylamino, n-hexylcarbonylamino, iodomethylcarbonylamino, ethylcarbonylamino, n-propylcarbonylamino, nfluoromethylcarbonylamino, bromomethylcarbonylamino,

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

A class of compounds of specific interest comprises those

q is an integer from 1 to 4;

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compounds of Formula I wherein:

hydrogen and (C<sub>1</sub>-C<sub>10</sub>)alkyl; or  $\mathbb{R}^{1}$  and  $\mathbb{R}^{2}$  are independently selected from the group consisting of

form (C3-C10)cycloalkyl; and  $\mathbb{R}^1$  and  $\mathbb{R}^2$  taken together with the carbon to which they are attached

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hydrogen and hydroxy; and  $m R^3$  and  $m R^4$  are independently selected from the group consisting of

heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; polyether; -OR  $^{13}$ ; -NR  $^{13}$ R  $^{14}$ ; and -NR  $^{13}$ C(O)R  $^{14}$ .  $halogen; \ hydroxy; -NO2; \ (C_i-C_{10})alkyl; \ halo(C_i-C_{10})alkyl; \ aryl(C_i-C_{10})alkyl; \ halo(C_i-C_{10})alkyl; \ halo(C_i-C_{10})alky$ or more radicals independently selected from the group consisting of R2 is phenyl, wherein said phenyl is optionally substituted with one

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wherein  $R^{13}$ ,  $R^{14}$ , and  $R^{15}$  are independently selected from the

 $C_{10}$ )alkyl;  $(C_1-C_{10})$ alkylammonium $(C_1-C_{10})$ alkyl; and polyether; or quaternary heterocyclyl; aryl( $C_1$ - $C_{10}$ )alkyl; heterocyclyl( $C_1$ - $C_{10}$ )alkyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylheterocyclyl(C<sub>1</sub>group consisting of hydrogen; (C<sub>r</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl;

and polyether radicals optionally may be substituted with one or more  $C_{10}$ )alkylheterocyclyl $(C_1-C_{10})$ alkyl;  $(C_1-C_{10})$ alkylammonium $(C_1-C_{10})$ alkyl; C10)alkyl; quaternary heterocyclyl(C1-C10)alkyl; (C1heterocyclyl; quaternary heterocyclyl; aryl(C1-C10)alkyl; heterocyclyl(C1wherein the R  $^{13}$ , R  $^{14}$ , and R  $^{15}$  (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl;

5 carboxy; carboxy(C;-C;0)alkyl; -OR  $^{16};$  -NR  $^9R$   $^{10};$  -N  $^+R$   $^9R$   $^{10}R$   $^WA$  ; and radicals selected from the group consisting of halogen; (C,-C10)alkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl;

5 consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; ammonium(C<sub>1</sub>-C10)alkyl; carboxyheterocyclyl; carboxy(C1-C10)alkylamino; and acyl; or  $heterocyclyl(C_1\text{-}C_{10})alkyl; carboxy(C_1\text{-}C_{10})alkyl; carbo(C_1\text{-}C_{10})alkoxy(C_1\text{-}C_{10})alkoxy(C_1\text{-}C_{10})alkyl; carboxy(C_1\text{-}C_{10})alkyl; carboxy(C_1\text{-}C_{10})alkyl$  $C_{10}$ )alkyl;  $(C_1-C_{10})$ alkylammonium $(C_1-C_{10})$ alkyl; aryl $(C_1-C_{10})$ alkyl; wherein A is a pharmaceutically acceptable anion; and wherein  $R^9$  and  $R^{10}$  are independently selected from the group

20  $carboxy(C_{i}\text{-}C_{10})alkyl; \ and \ carbo(C_{i}\text{-}C_{10})alkoxy(C_{i}\text{-}C_{10})alkyl; \ or \ although \ and \ carboxy(C_{i}\text{-}C_{i0})alkyl; \ or \ although \ and \ although \ and \ although \ although \ although \ although \ and \ although \ alt$ consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl;  $\mathbb{R}^{11}$  and  $\mathbb{R}^{12}$  together with the carbon atom to which they are wherein  $\mathbb{R}^{11}$  and  $\mathbb{R}^{12}$  are independently selected from the group

25 compounds of Formula I; and wherein R" and R16 are as previously set forth above for the

attached form a cyclic ring; and

R6 is hydrogen; and

and aryl(C1-C10)alkyl; and  $\mathbb{R}^N$  is selected from the group consisting of hydrogen; (C,-C,0)alkyl;

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one or more RX radicals are independently selected from the group consisting of hydrogen; -NO2; (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; -OR $^{13}$ ; -NR 13R 14.

wherein R13 and R14 are as defined above; or

provided that aryl is selected from the group consisting of optionally a pharmaceutically acceptable salt, solvate, or prodrug thereof; and substituted phenyl, biphenyl and naphthyl; and

optionally substituted heterocyclyl comprising a 5 to 10 membered ring and comprising one or more ring atoms that are heteroatoms selected from the provided that heterocyclyl is selected from the group consisting of group consisting of oxygen, nitrogen, sulfur and phosphorus.

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A class of compounds of high interest comprises those compounds of Formula I wherein:

q is an integer from 1 to 4;

 $R^{1}$  and  $R^{2}$  are independently selected from the group consisting of ethyl and n-butyl; or 13

R 1 and R 2 taken together with the carbon to which they are attached form cyclopentyl; and

one of R3 and R4 is hydrogen and the other of R3 and R4 is

 hydroxy; and ឧ

diethylaminophenyl, trimethylammoniumphenyl, triethylammoniumphenyl, R<sup>5</sup> is selected from the group consisting of phenyl, hydroxyphenyl, methylaminophenyl, dimethylaminophenyl, ethylaminophenyl, methoxyphenyl, ethoxyphenyl, nitrophenyl, aminophenyl,

trimethylammoniummethylcarbonylaminophenyl, triethylammoniummethylcarbonylaminophenyl, trimethylammoniumethylcarbonylaminophenyl, triethylammoniumethylcarbonylaminophenyl, 22

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trimethylammoniumpropylcarbonylaminophenyl, trimethylammoniumbutylcarbonylaminophenyl, triethylammoniumpropylcarbonylaminophenyl,

triethylammoniumbutylcarbonylaminophenyl, methylcarbonylaminophenyl, chloromethylcarbonylaminophenyl, fluoromethylcarbonylaminophenyl, bromomethylcarbonylaminophenyl, iodomethylcarbonylaminophenyl, fluoroethyłcarbonylaminophenyl, bromoethylcarbonylaminophenyl. ethylcarbonylaminophenyl, chloroethylcarbonylaminophenyl,

iodoethylcarbonylaminophenyl, propylcarbonylaminophenyl,

- chloropropylcarbonylaminophenyl, fluoropropylcarbonylaminophenyl, bromopropylcarbonylaminophenyl, iodopropylcarbonylaminophenyl, fluorobutylcarbonylaminophenyl, bromobutylcarbonylaminophenyl, outylearbonylaminophenyl, chlorobutylearbonylaminophenyl, iodobutylcarbonylaminophenyl, 2
- bromoethoxyethoxyethoxyphenyl, iodoethoxyethoxyethoxyphenyl, and chloroethoxyethoxyethoxyphenyl, fluoroethoxyethoxyethoxyphenyl, trimethylammoniumethoxyethoxyethoxyphenyl, triethylammoniumethoxyethoxyethoxyphenyl, pyridiniumethoxyethoxyethoxyphenyl; and 2
- R' is hydrogen; ន

 $\mathbb{R}^{N}$  is selected from the group consisting of hydrogen, methyl, ethyl, and benzyl; and one or more RX radicals are independently selected from the group hydroxyamino, methylamino, dimethylamino, ethylamino, diethylamino, trimethylammonium, triethylammonium, N-methyl-N-carboxymethylconsisting of hydroxy, methyl, ethyl, methoxy, ethoxy, amino,

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amino, N,N-dimethyl-N-carboxymethyl-ammonium, methylcarbonylamino, chloromethylcarbonylamino, fluoromethylcarbonylamino bromomethylcarbonylamino, iodomethylcarbonylamino,

ethylcarbonylamino, benzyloxycarbonylamino, and aminoimidocarbonylamino; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

compounds of Formula I wherein: A subclass of compounds of high interest comprises those

wherein:

q is 1 or 2;

R l and R2 are each independently alkyl;

R<sup>3</sup> is hydroxy;

R<sup>5</sup> has the formula (II): R<sup>4</sup> and R<sup>6</sup> are hydrogen;

wherein t is an integer from 0 to 5;

of hydrogen; halogen; -CN; -NO2; oxo; alkyl; polyalkyl; haloalkyl; one or more RY are independently selected from the group consisting

20 15 NR"SO2NR"R"; -P(O)R 13R 14; -PR 13R 14; -P+R 13R 14R 15A; -OC(O)NR13R14; -NR13SOR14; -NR13SO<sub>2</sub>R14; -NR13SONR14R15; hydroxyalkyi; cycloalkyi; alkenyi; alkynyi; aryi; heterocyclyi; quaternary P(OR 13)OR 14; -S+R 13R 14A; and -N+R 13R 14R 15A; and COR<sup>13</sup>; -NR<sup>13</sup>C(O)R<sup>14</sup>; -NR<sup>13</sup>C(O)NR<sup>14</sup>R<sup>15</sup>; -NR<sup>13</sup>CO<sub>2</sub>R<sup>14</sup>; -OC(O)R<sup>15</sup>; -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; -OR 13; -NR 13R 14  $CO_2R^{13}$ ; -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>; -C(O)NR<sup>13</sup>R<sup>14</sup>; -C(O)OM;

> consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; P(O)(OR')OR'; and may be further substituted with one or more radicals selected from the group CONR 7R8; -N+R7R8R9A-; -P(O)R7R8; -PR7R8; -P+R7R8R9A; and heterocyclyl;  $-OR^7$ ;  $-NR^7R^8$ ;  $-SR^7$ ;  $-S(O)R^7$ ;  $-SO_2R^7$ ;  $-SO_3R^7$ ;  $-CO_2R^7$ ; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl, and polyether substituents of the RY radicals optionally alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl,

20 15 5 alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; SO-; -SO2-; -S<sup>+</sup>R<sup>7</sup>A-; -PR<sup>7</sup>-; -P(O)R<sup>7</sup>-; -P<sup>+</sup>R<sup>7</sup>R<sup>8</sup>A-; or phenylene; and may have one or more carbons replaced by -O-; -NR $^7$ -; -N $^+$ R $^7$ R $^8$ A--; -S-; heterocyclylalkyl, and polyether substituents of the RY radicals optionally alkenyi, alkynyi, aryi, heterocyclyi, quaternary heterocyclyi, aryialkyi, alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, wherein  $\mathbb{R}^7$  and  $\mathbb{R}^8$  are independently selected from the group wherein  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  are independently selected from the

23 are attached form a mono- or polycyclic heterocyclyl that is optionally oxo, carboxy, and quaternary salts; or substituted with one or more radicals selected from the group consisting of wherein  $\mathbb{R}^{14}$  and  $\mathbb{R}^{15}$  together with the nitrogen atom to which they wherein R13 and R14 together with the nitrogen atom to which they

are attached form a cyclic ring; and

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wherein the R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> alkyl; haloalkyl; cycloalkyl; polyalkyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylarmoniumalkyl; aminocarbonylalkyl;

- alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; -OR <sup>16</sup>, -NR <sup>9</sup>R <sup>10</sup>, -N<sup>+</sup>R <sup>9</sup>R <sup>10</sup>R M <sup>-</sup>; -SR <sup>16</sup>, -S(O)R <sup>9</sup>, -SO<sub>2</sub>R <sup>16</sup>; -CO<sub>2</sub>R <sup>16</sup>; -CONR <sup>9</sup>R <sup>10</sup>, -SO<sub>2</sub>NR <sup>9</sup>R <sup>10</sup>, -PO(OR <sup>16</sup>)OR <sup>17</sup>; -SO<sub>2</sub>R <sup>10</sup>, -PO(OR <sup>16</sup>)OR <sup>17</sup>; -PO(OR
  - guanidinyl; -OR<sup>16</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>w</sup>A<sup>-</sup>; -SR<sup>16</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>16</sup>; -CO<sub>2</sub>R<sup>16</sup>; -CONR<sup>9</sup>R<sup>10</sup>; -SO<sub>2</sub>NR<sup>9</sup>R<sup>10</sup>; -PO(OR<sup>16</sup>)OR<sup>17</sup>; -PR<sup>9</sup>R<sup>10</sup>; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>11</sup>A-; -S<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-; and carbohydrate residue; and wherein the R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alynyl; aryl; heterocyclyl; quaternary heterocyclyl;
    arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl;
    - arylalkyl; heterocyclylalkyl; quatemary heterocyclylalkyl; alkylarylalkyl;
       alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl;
       alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O.; -NR\*; N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-; -SO.; -SO.; -SO.; -S<sup>+</sup>R<sup>9</sup>A-; -PR<sup>9</sup>; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-; -P(O)R\*.
- polypeptide residue; and wherein R  $^{16}$  and R  $^{17}$  are independently selected from the group consisting of R  $^{9}$  and M; and

phenylene; carbohydrate residue; amino acid residue; peptide residue; or

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wherein M is a pharmaceutically acceptable cation; and

wherein R', R'', R'', R'', R'', and A' are as previously set forth above for the compounds of Formula I; and

 $\mathbb{R}^N$  is selected from the group consisting of hydrogen; alkyl; and aralkyl: and

one or more Rx radicals are independently selected from the group

;

consisting of alkoxy, alkylamino and dialkylamino; or a pharmaceutically acceptable salt, solvate, or prodrug thereof.

A family of specific compounds of particular interest within Formula I consists of the following compounds:

5 (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4R,5R)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-1,2-benzothiazzepin-4-ol 1,1-dioxide;

10 5-chloro-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]pentanamide;

5-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-N.N.N-triethyl-5-oxo-pentanaminium trifluoroacetate;

15 2-chloro-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]acetamide;

2-[[3-[(4K,5R)-3,3-dibutyl-7-(dimethylamino]-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-N,N,N-triethyl-2-oxoethanaminium chloride;

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(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

hydroxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide; (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-

iodoethyoxy)ethoxy)ethoxy)phenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-(((2-

hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5yl]phenoxy]ethoxy]ethyl]pyridinium; 1-[2-[2-[4-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-

ಕ 2-[2-[4-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4yl]phenoxy]ethoxy]-N,N,N-triethylethanaminium iodide; hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-

methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide; (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-

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(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,2-benzothiazepin-4-ol 1,1-dioxide and (45,5R)-3,3-dibuty1-7-(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-

(4R,5R)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-1,2-benzothiazepin-4-ol 1,1-dioxide;

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hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl)phenyl]pentanamide; 5-bromo-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-

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pentanaminium trifluoroacetate; 1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-N,N,N-triethyl-5-oxo-1-5-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-phenyl-1,2-

benzothiazepin-4-ol 1,1-dioxide;

methoxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide; (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-

hydroxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide; (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-

<del>-</del>0 2-[2-[4-[(4R,5R)-3,3-dibutyl-7- (dimethylamino)-2,3,4,5-tetrahydro-4triethylethanaminium iodide; hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]-N,N,N-

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-2-

15 (phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4R,5R)-3,3-dibuty1-7-(dimethylamino)-5-[3-(ethylamino)phenyl]-2,3,4,5tetrahydro-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4methoxyphenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide; and

20 spiro[1,2-benzothiazepine-3(2H),1'-cyclopentan]-4-ol 1,1-dioxide; and (4R,5R)-7-dimethylamino)-2-ethyl-4,5-dihydro-5-(4-methoxyphenyl)-

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the pharmaceutically-acceptably salts thereof.

The invention further comprises a compound selected from among:

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wherein R<sup>19</sup> is selected from the group consisting of alkane diyl, alkene diyl, alkyne diyl, polyalkane diyl, alkoxy diyl, polyether diyl, polyalkoxy diyl, carbohydrate residue, amino acid residue, peptide residue, and polypeptide residue; and

wherein alkane diyl, alkene diyl, alkyne diyl, polyalkane diyl, alkoxy
diyl, polyether diyl, polyalkoxy diyl, carbohydrate residue, amino acid residue,
peptide residue, and polypeptide residue optionally may have one or more
carbon atoms replaced by -O-, -NR?, -N\*R?R\*A-, -S-, -SO-, -SO, -S\*R?A-,
PR?-, -PR?R\*A-, phenylene, heterocyclyl, quaternary heterocyclyl, or aryl;

15 diyl, polyether diyl, polyalkoxy diyl, carbohydrate residue, amino acid residue, peptide residue, and polypeptide residue optimally can be substituted with one

wherein alkane diyl, alkene diyl, alkyne diyl, polyalkane diyl, alkoxy

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or more radicals independently selected from the group consisting of alkyl, alkcnyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocyclyl, arylalkyl, halogen, oxo, -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -NO<sub>2</sub>; -CO<sub>2</sub>R<sup>13</sup>; -CK); -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>OM; -CO)NR<sup>13</sup>R<sup>14</sup>; -C(O)NR<sup>13</sup>R<sup>14</sup>; -C(O)OM; -COR<sup>13</sup>; -P(O)R<sup>13</sup>R<sup>14</sup>; -PR<sup>13</sup>R<sup>14</sup>R<sup>14</sup>; -PR<sup>13</sup>R<sup>14</sup>R<sup>14</sup>R<sup>13</sup>R<sup>14</sup>; -PR<sup>13</sup>R<sup>14</sup>R<sup>14</sup>R<sup>13</sup>R<sup>14</sup>; -PR<sup>13</sup>R<sup>14</sup>R<sup>14</sup>R<sup>15</sup>A<sup>1</sup>; -PR<sup>13</sup>R<sup>14</sup>R<sup>14</sup>A<sup>1</sup>; -P(OR<sup>13</sup>)OR<sup>14</sup>; -S'R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>1</sup>;

wherein  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$ , M and  $A^{c}$  are as previously set forth above for the compounds of Formula I; and

wherein R<sup>19</sup> can further comprise functional linkages by which R<sup>19</sup> is bonded to R<sup>20</sup> and/or R<sup>21</sup> in the compounds of Formula DI; to R<sup>20</sup>, R<sup>21</sup> and/or R<sup>21</sup> in the compounds of Formula DII; and to R<sup>20</sup>, R<sup>21</sup>, R<sup>22</sup> and/or R<sup>23</sup> in the compounds of Formula DIII; and

wherein each of R<sup>20</sup>, R<sup>21</sup>, or R<sup>22</sup> and R<sup>23</sup> comprises a benzothiazepine 15 moiety as described above that is therapeutically effective in inhibiting ileal bile acid transport.

Exemplary R<sup>19</sup> substituents include, but are not limited to, the illowing:

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· R<sup>25</sup> is selected from the group consisting of carbon and nitrogen; and R4, R27, R41, R42, R10, R11, R12, R13, R14, R13, R14, and R37 are

independently selected from the group consisting of:

and heterocyclylalkyl; consisting of alkyl, alkenyl, alkylaryl, aryl, arylalkyl, cycloalkyl, heterocyclyl, wherein  $R^{38}$  ,  $R^{39}$  ,  $R^{40}$  and  $R^{41}$  are independently selected from the group

A' is a pharmaceutically acceptable anion; and

integers from 1 to 10 inclusive. h, i, j and k are independently selected from the group consisting of

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 $\mathbb{R}^{2}$  comprises a benzothiazepine moiety corresponding to the Formula DIV or Formula DI, Formula DII and Formula DIII in which each of  $R^{20},\,R^{21},\,R^{22}$  and The invention is also directed to a compound selected from among Formula DIVA:

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wherein R¹, R², R³, R⁴, R⁵, Rk, Rx, q, and n are as previously defined above for the compounds of Formula I, and R33 is either a covalent bond or arylene.

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In compounds of Formula DIV, it is particularly preferred that each of position to R19. In compounds of Formula DIVA, it is particularly preferred that  $\mathbb{R}^{35}$  comprise a phenylene moiety bonded at a m- or p-carbon thereof to R20, R21, R22, and R22 in Formulae DI, DII and DIII be bonded at its 7- or 8-.

Examples of Formula DI include:

and

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among other combinations, ethyl/butyl or butyl/butyl. definitions as stated above for R1, R2, R3, R4, R44, R7, RX, q and t, respectively. In any of the compounds of the present invention, R1 and R2 can be, Illustrative dimeric compounds include the following: wherein R1A, R2A, R3A, R4A, RNA, RYA, RXA, r and u have the same

In another embodiment, a core moiety backbone, R<sup>19</sup>, as discussed herein in Formulae DI, DII and DIII can be multiply substituted with more than four pendant active benzothiazepine units, i.e., R<sup>20</sup>, R<sup>21</sup>, R<sup>22</sup>, and R<sup>23</sup> as discussed above, through multiple functional groups within the core moiety backbone unit, R<sup>19</sup>, can comprise a single core moiety unit, multimers thereof, and multimeric mixtures of the different core moiety units discussed herein, i.e., alone or in combination. The number of individual core moiety backbone units can range from about one to about 100, preferably about one to about 80, more preferably about one to about 50, and even more preferably about one to about 25. The number of points of

can include bonds to C, S, O, N, or P within any of the groups encompassed by the definition of R!?

The more preferred benzothiazepine moieties comprising R<sup>29</sup>, R<sup>21</sup>, R<sup>22</sup> and/or R<sup>23</sup> conform to the preferred structures as outlined above for Formula I. The 3-position carbon on each benzothiazepine moiety can be achiral, and the substituents R¹, R², R², R², R³ and R² can be selected from the preferred groups and combinations of substituents as discussed above. The core structures can comprise, for example, poly(oxyalkylene) or oligo(oxyalkylene), especially

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#### Methods of Treatment

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poly- or oligo(oxyethylene) or poly- or oligo(oxypropylene).

In another aspect, the present invention provides a pharmaceutical composition for the prophylaxis and/or treatment of a disease, condition and/or disorder for which a bile acid transport inhibitor is indicated, such as a hyperlipidemic condition, for example, atherosclerosis. Such compositions

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comprise any of the compounds disclosed above, alone or in combination, in an amount effective to reduce bile acid levels in the blood, or to reduce transport thereof across digestive system membranes, alone or in a composition comprising, for example, one or more pharmaceutically acceptable carriers,

excipients, and/or diluents. In any of the dimeric or multimeric structures discussed immediately above, for example, the benzothiazzpine compounds of the present invention can be used alone or in various combinations.

In a further aspect, the present invention also provides a method of treating a disease, condition and/or disorder in mammals, including humans, for which a bile acid transport inhibitor is indicated, comprising administering to a patient in need thereof a compound of the present invention in an effective

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amount in unit dosage form or in divided doses.

attachment of similar or different pendant active benzothiazepine units within a

100, preferably about one to about 80, more preferably about one to about 50,

and even more preferably about one to about 25. Such points of attachment

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single core moiety backbone unit can be in the range from about one to about

In yet a further aspect, the present invention comprises the use of the compounds of Formula I and/or the dimeric or multimeric compounds of Formulae DI, DII and/or DIII in the preparation of a medicament useful for the prophylaxis and/or treatment of a disease, condition and/or disorder for which a bile acid transport inhibitor is indicated.

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The compounds of Formula I are also useful for the prophylaxis and/or treatment of gallstones.

20 In yet a further aspect, the present invention also provides processes for the preparation of compounds of the present invention. Further scope of the applicability of the present invention will become apparent from the detailed description provided below. However, it should be understood that the following detailed description and examples, while

indicating preferred embodiments of the invention, are given by way of illustration only since various changes and modifications within the spirit and scope of the invention will beomee apparent to those skilled in the art from this denaited description

#### Definitions and Abbreviations

description, the following definitions are provided: In order to aid the reader in understanding the following detailed

alkenaryl and alkynaryl. Preferably, these moieties comprise 1 to 20 carbon substituted with other aliphatic or cyclic hydrocarbon groups, such as alkaryl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, and aryl moieties. These radicals also include alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, and aryl moieties elements carbon and hydrogen. These radicals include, for example, alkyl, The term "hydrocarbyl" refers to radicals consisting exclusively of the

chain atom is replaced with a heteroatom such as nitrogen, oxygen, sulfur, or a Substituted hydrocarbyl also includes hydrocarbyl radicals in which a carbon hydroxy; protected hydroxy; acyl; acyloxy; nitro; cyano; amino; and amido. acetals; ketals; esters, heterocyclyl such as furyl and thienyl; alkanoxy; methoxy, ethoxy, and butoxy; halogen such as chloro and fluoro; ethers; substituted with groups such as, but not limited to, lower alkoxy such as Examples of such substituted hydrocarbyl include hydrocarbyl radicals as but not limited to, halogen, oxygen, nitrogen, sulfur and phosphorus. is substituted with a group comprising at least one atom other than carbon, such The term "substituted hydrocarbyl" refers to a hydrocarbyl radical that

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one to about six carbon atoms. Examples of such radicals include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isoone to three carbon atoms amyl, hexyl and the like. Even more preferred are lower alkyl radicals having carbon atoms. More preferred alkyl radicals are "lower alkyl" radicals having having one to about twenty carbon atoms or, preferably, one to about twelve as "haloalkyl", and "hydroxyalkyl", it embraces linear or branched radicals Where the term "alkyl" is used, either alone or within other terms such

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such as "arylalkenyl", it embraces linear or branched radicals having at least Where the term "alkenyl" is used, either alone or within other terms

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methylbutenyl. of alkenyl radicals include ethenyl, propenyl, allyl, propenyl, butenyl and 4are "lower alkenyl" radicals having two to about six carbon atoms. Examples preferably, two to about twelve carbon atoms. More preferred alkenyl radicals one carbon-carbon double bond of two to about twenty carbon atoms or,

and "trans" orientations, or alternatively, "B" and "Z" orientations. The terms "alkenyl" and "lower alkenyl", embrace radicals having "cis' S

to about six carbon atoms. Examples of such radicals include propargyl, More preferred alkynyl radicals are "lower alkynyl" radicals having two to about ten carbon atoms. Most preferred are lower alkynyl radicals having two butynyl, and the like. about twenty carbon atoms or, preferably, two to about twelve carbon atoms The term "alkynyl" denotes linear or branched radicals having two to

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8 2 three to about twelve carbon atoms. More preferred cycloalkyl radicals are heterocyclic ring of the benzothiazepine. cycloalkyl ring has a carbon ring atom in common with the seven-membered of such radicals include cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. The term "cycloalkyl" additionally encompasses spiro systems wherein the "lower cycloalkyl" radicals having three to about ten carbon atoms. Examples The term "cycloalkyl" embraces saturated carbocyclic radicals having

cyclopentenyl and cyclohexenyl. preferred cycloalkenyl radicals are "lower cycloalkenyl" radicals having four to partially unsaturated carbocyclic radicals that contain two double bonds (that about ten carbon atoms. Examples of such radicals include cyclobutenyl, may or may not be conjugated) can be called "cycloalkyldienyl". More radicals having three to twelve carbon atoms. Cycloalkenyl radicals that are The term "cycloalkenyl" embraces partially unsaturated carbocyclic

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wherein any one or more of the alkyl carbon atoms is substituted with halo as chlorine, bromine or iodine atoms. The term "haloalkyl" embraces radicals The term "halo" and "halogen" means halogens such as fluorine,

defined above. Specifically embraced are monohaloalkyl, dihaloalkyl and polyhaloalkyl radicals. A monohaloalkyl radical, for one example, may have either an iodo, bromo, chloro or fluoro atom within the radical. Dihalo and polyhaloalkyl radicals may have two or more of the same halo atoms or a combination of different halo radicals. "Lower haloalkyl" embraces radicals having one to six carbon atoms. Examples of haloalkyl radicals include fluoromethyl, difluoromethyl, trichloromethyl, difluoroethyl, difluoropropyl, difluorochloromethyl, dichloroethyl, and dichlorofluoromethyl, means alkyl radicals having all hydrogen atoms replaced with fluoro atoms. Examples include trifluoromethyl and pentafluoroethyl.

The term "hydroxyalkyl" embraces linear or branched alkyl radicals having one to about ten carbon atoms any one of which may be substituted with one or more hydroxyl radicals. More preferred hydroxyalkyl radicals are "lower hydroxyl radicals having one to six carbon atoms and one or more hydroxyl radicals. Examples of such radicals include hydroxymethyl, hydroxypropyl, hydroxybutyl and hydroxyhexyl. Even more preferred are lower hydroxyakyl radicals having one to three carbon atoms.

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20 The term "aryl", alone or in combination, means a carbocyclic aromatic system containing one or more rings wherein such rings may be attached together in a pendent manner or may be fused. The term "aryl" embraces aromatic radicals such as phenyl, naphthyl, tetrahydronaphthyl, indane, biphenyl, and anthracenyl. More preferred aryl is phenyl. Said "aryl" group may have one to three substituents such as lower alkyl, hydroxy, halo, haloalkyl, nitro, cyano, alkoxy and lower alkylamino.

The term "heterocyclyl" embraces saturated, partially saturated and unsaturated heteroatom-containing ring-shaped radicals, where the heteroatoms may be selected from nitrogen, sulfur and oxygen. Preferred heterocyclyl are 3-10 membered ring heterocyclyl, particularly 5-8 membered ring heterocyclyl.

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Examples of saturated heterocyclic radicals include saturated 3 to 6-membered heteromonocyclic groups containing 1 to 4 nitrogen atoms [e.g. pyrrolidinyl, imidazolidinyl, piperidino, piperazinyl]; saturated 3 to 6-membered heteromonocyclic groups containing 1 to 2 oxygen atoms and 1 to 3 nitrogen

- atoms [e.g. morpholinyl]; saturated 3 to 6-membered heteromonocyclic groups containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., thiszolidinyl].

  Examples of partially saturated heterocyclyl radicals include dihydrothiophene, dihydropyran, dihydrofuran and dihydrothiazole. Examples of unsaturated heterocyclic radicals, also termed "heteroaryl" radicals, include unsaturated 5
  - 10 to 6 membered heteromonocyclyl groups containing 1 to 4 nitrogen atoms, for example, pyrrolinyl, imidazolyl, pyrazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl [e.g., 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl]; unsaturated condensed heterocyclic groups containing 1 to 5 nitrogen atoms, for example, indolyl, isoindolyl, indolizinyl,
    - benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl, tetrazolopyridazinyl [e.g., tetrazolo [1,5-b]pyridazinyl]; unsaturated 3 to 6-membered heteromonocyclic groups containing an oxygen atom, for example, pyranyl, 2-furyl, 3-furyl, etc.; unsaturated 5 to 6-membered heteromonocyclic groups containing a sulfur atom, for example, 2-thienyl, 3-thienyl, etc.;
      - unsaturated 5- to 6-membered heteromonocyclic groups containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, isoxazolyl, oxadiazolyl [e.g., 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl]; unsaturated condensed heterocyclic groups containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. benzoxazolyl, benzoxadiazolyl]; unsaturated 5 to 6-
- membered heteromonocyclic groups containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms, for example, thiazolyl, thiadiazolyl [e.g., 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl); unsaturated condensed heterocyclic groups containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., benzothiazolyl, benzothiadiazolyl] and the like. The term also embraces
- 30 radicals where heterocyclic radicals are fused with aryl radicals. Examples of

5 one or two heteroatoms selected from sulfur nitrogen and oxygen, selected 3-10 membered fused or unfused radicals. Preferred examples of heteroaryl pyridyl, piperidinyl and pyrazinyl. from thienyl, furanyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, More preferred heteroaryl radicals are 5- or 6-membered heteroaryl, containing benzodioxolyl, benzodioxanyl, pyridyl, thienyl, thiazolyl, furyl, and pyrazinyl dihydroindolyl, chromanyl, benzopyran, thiochromanyl, benzothiopyran, radicals include benzofuryl, 2,3-dihydrobenzofuryl, benzothienyl, indolyl, Heterocyclic radicals can include fused or unfused radicals, particularly

The term "heteroaryl" means a fully unsaturated heterocyclyl

molecule of interest can be at the heteroatom or elsewhere within the ring. In either "heterocyclyl" or "heteroaryl," the point of attachment to the

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heterocyclyl and heteroaryl which contain more than one ring heteroatom and said heterocyclyl and heteroaryl. for which isomers are possible, such isomers are included in the definition of The term "triazolyl" includes all positional isomers. In all other

25 20 the molecule of interest can be at a heteroatom or elsewhere. charged structures). The point of attachment of the quaternary heterocyclyl to the term is intended to encompass both ternary and quaternary positively oxygen, has such a number of bonds that it is positively charged (and therefore or more of the heteroatoms, for example, nitrogen, sulfur, phosphorus or The term "quaternary heterocyclyl" means a heterocyclyl in which one

structures). The point of attachment of the quaternary heteroaryl to the has such a number of bonds that it is positively charged (and therefore the term more of the heteroatoms, for example, nitrogen, sulfur, phosphorus or oxygen, is intended to encompass both temary and quaternary positively charged The term "quaternary heteroary!" means a heteroary! in which one or

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molecule of interest can be at a heteroatom or elsewhere

points of attachment to molecules of interest The term "diyl" means a diradical moiety wherein said moiety has two

The term "oxo" means a doubly bonded oxygen

having a molecular weight up to about 20,000, more preferably up to about 10,000, and most preferably up to about 5,000. The term "polyalkyl" means a branched or straight hydrocarbon chain

about 20,000, more preferably up to about 10,000, and most preferably up to are replaced by oxygen, wherein the polyether has a molecular weight up to The term "polyether" means a polyalkyl wherein one or more carbons

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to about 10,000, and most preferably up to about 5,000 the polyalkoxy has a molecular weight up to about 20,000, more preferably up The term "polyalkoxy" means a polymer of alkylene oxides, wherein

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propanediol, glucaric acid and galactaric acid. sedoheptulose, glucosamine, galactosamine, glucoronic acid, galacturonic acid glucose, mannose, fructose, galactose, ribose, crythrose, glycerinaldehyde, and which belong to the D- or L-series; aminosugars; sugar alcohols; and up to about 20,000, for example, hydroxypropyl-methylcellulose or chitosan polysaccharides wherein the polysaccharides can have a molecular weight of gluconic acid, galactonic acid, mannoic acid, glucamine, 3-amino-1,2saccharic acids. Nonlimiting specific examples of such carbohydrates include residue; compounds derived from aldoses and ketoses with 3 to 7 carbon atoms carbohydrates such as, but is not limited to, mono-, di-, tri-, tetra- and The term "carbohydrate residue" encompasses residues derived from

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to about 100 amino acid units The term "peptide residue" means polyamino acid residue containing up 25

more preferably from about 100 amino acid units to about 750 amino acid containing from about 100 amino acid units to about 1000 amino acid units The term "polypeptide residue" means a polyamino acid residue

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untis, and most preferably from about 100 amino acid units to about 500 amino

The term "alkylammoniumalkyl" means an an -NH3, group or a mono-di- or tri-substituted amino group, any of which is bonded to an alkyl wherein said alkyl is bonded to the molecule of interest.

The term "sulfo" means a sulfo group, -SO3H, and its salts.

The term "sulfoalkyl" means an alkyl group to which a sulfonate group is bonded, wherein said alkyl is bonded to the molecule of interest.

The term "aralkyl" embraces aryl-substituted alkyl radicals. Preferable aralkyl radicals are "lower aralkyl" radicals having aryl radicals attached to alkyl radicals having one to six carbon atoms. Even more preferred are lower aralkyl radicals having phenyl attached to alkyl portions having one to three carbon atoms. Examples of such radicals include benzyl, diphenylmethyl and phenylethyl. The aryl in said aralkyl may be additionally substituted with halo, alto a silvent believed to alkyl may be additionally substituted with halo, alto a silvent believed to alkyl may be additionally substituted with halo, alto a silvent believed to alkyl may be additionally substituted with halo, alto a silvent believed to alkyl may be additionally substituted with halo, alto a silvent believed to alkyl may be additionally substituted with halo, alto a silvent believed to alkyl may be additionally substituted with halo, alto a silvent believed to alkyl may be additionally substituted with halo, alto a silvent believed to alto a silvent believed to alto a silvent believed to a s

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alkyl, alkoxy, halkoalkyl and haloalkoxy. The term "arylalkernyl" embraces aryl-substituted alkenyl radicals. Preferable arylalkenyl radicals are "lower arylalkenyl" radicals having aryl radicals attached to alkenyl radicals having The term "heterocyclylalkyl" means an alkyl radical that is substituted

with one or more heterocyclyl groups. Preferable heterocyclylalkyl radicals are
"lower heterocyclylalkyl" radicals having one or more heterocyclyl groups
attached to an alkyl radical having one to ten carbon atoms.

The term "heteroary/alkyl" means an alkyl radical that is substituted with one or more heteroaryl groups. Preferable heteroarylalkyl radicals are "lower heteroarylalkyl" radicals having one or more heteroaryl groups attached to an alkyl radical having one to ten carbon atoms.

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The term "quaternary heterocyclylalkyl" means an alkyl radical that is substituted with one or more quaternary heterocyclyl groups. Preferable quaternary heterocyclylalkyl radicals are "lower quaternary heterocyclylalkyl" radicals having one or more quaternary heterocyclyl groups attached to an alkyl radical having one to ten carbon atoms.

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The term "quaternary heteroarylalkyl" means an alkyl radical that is substituted with one or more quaternary heteroaryl groups. Preferable quaternary heteroarylalkyl radicals are "lower quaternary heteroarylalkyl" radicals having one or more quaternary heteroaryl groups attached to an alkyl radical having one to ten carbon atoms.

The term "alkylheteroarylalkyl" means a heteroarylalkyl radical that is substituted with one or more alkyl groups. Preferable alkylheteroarylalkyl radicals are "lower alkylheteroarylalkyl" radicals with alkyl portions having one to ten carbon atoms.

10 The term "alkoxy" means an alkyl radical which is attached to the molecule of interest by oxygen, such as a methoxy radical. More preferred alkoxy radicals are "lower alkoxy" radicals having one to six carbon atoms. Examples of such radicals include methoxy, ethoxy, propoxy, iso-propoxy, butoxy and tert-butoxy.

The term "carboxy" means the carboxy group, -CO,H, or its salts.

The term "carboxyalkyl" means an alkyl radical that is substituted with one or more carboxy groups. Preferable carboxyalkyl radicals are "lower carboxyalkyl" radicals having one or more carboxy groups attached to an alkyl radical having one to six carbon atoms.

20 The term "carboxyheterocyclyl" means a heterocyclyl radical that is substituted with one or more carboxy groups.

The term "carboxyheteroary!" means a heteroaryl radical that is substituted with one or more carboxy groups.

The term "carboalkoxyalkyl" means an alkyl radical that is substituted with one or more alkoxycarbonyl groups. Preferable carboalkoxyalkyl radicals are "lower carboalkoxyalkyl" radicals having one or more alkoxycarbonyl groups attached to an alkyl radical having one to six carbon atoms.

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The term "carboxyalkylamino" means an amino radical that is mono- or di-substituted When used in combination, for example "alkylaryl" or

30 "arylalkyl," the individual terms listed above have the meaning indicated

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above.

not limited to, acetyl and benzoyl. the carboxy group has been removed. Examples of acyl groups include, but are The term "acyl" means an organic acid group in which the hydroxy of

invention that inhibits transport of bile acids The term "active compound" means a compound of the present

of a mammal, such as a human. This includes increasing the fecal excretion of inhibiting absorption of bile acids from the intestine into the circulatory system The term "a bile acid transport inhibitor" means a compound capable of

5 prophylaxis and/or treatment by bile acid transport inhibition include, for cholesterol and cholesterol ester, and more specifically, reducing LDL and bile acids, as well as reducing the blood plasma or serum concentrations of VLDL cholesterol. Conditions and/or diseases that benefit from the example, a hyperlipidemic condition such as atherosclerosis.

15 The term "THF" means tetrahydrofuran; The abbreviations used in this application have the following meanings:

The term "PTC" means phase transfer catalyst;

The term "Aliquart 336" means methyltricaprylylammonium chloride;

The term "MCPBA" means m-chloroperbenzoic acid;

20 The term "Celite" refers to a brand of diatomaceous earth filtering aid; The term "DMF" means dimethylformamide;

The term "DME" means ethylene glycol dimethyl ether,

The term "BOC" means t-butoxycarbonyl;

The term "Me" means methyl;

The term "Et" means ethyl;

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The term "Bu" means butyl;

The term "EtOAc" means ethyl acetate;

The term "Et,O" means diethyl ether;

The term "LAH" means lithium aluminum hydride;

The term "KOSiMe," means potassium trimethylsilanolate; The term "DMSO" means dimethylsulfoxide;

The term "MS" means mass spectrometry;

The term "PEG" means polyethylene glycol;

The term "ES" means electrospray; The term "HRMS" means high resolution mass spectrometry;

The term "GC" means gas chromatography; The term "NMR" means nuclear magnetic resonance spectroscopy;

The term "MPLC" means medium pressure liquid chromatography;

chromatography The term "RPHPLC" means reverse phase high pressure liquid The term "HPLC" means high pressure liquid chromatography;

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The terms "h" or "hr" means hour(s); and The term "RT" means room temperature;

15 The term "min" means minute(s);

#### Alternate Forms of Compounds

such as diastereomers and enantiomers, in both pure form and in admixture. asymmetrical carbon atoms, and therefore include racemates and stereoisomers, The compounds of the present invention can have at least two

25 20 invention. bond. All such isomers are contemplated among the compounds of the present isomers of compounds of the present invention. Isomers may include techniques, either by reacting enantiomeric starting materials, or by separating geometric isomers, for example cis isomers or trans isomers across a double Such stereoisomers can be prepared and separated using conventional

solvates and prodrugs of such compounds. The compounds of the present invention also include tautomers, salts,

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Compound Syntheses

The starting materials for use in the preparation of the compounds of the invention are commercially available or can be prepared by conventional methods known to a skilled person or in an analogous manner to processes described in the art. Generally, the compounds of the present invention can be prepared by the procedures described below.

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- substituted benzenesulfonamide 5 is then successively reacted with (i) a strong substituted benzenesulfonamide 5. Protected benzenesulfonamide 4 or Nsuch as sodium hydride, in a solvent, such as dimethylformamide, to yield N. treated with an alkyl halide, such as methyl iodide, in the presence of a base benzenesulfonamide 4. Protected benzenesulfonamide 4 optionally can be
- 5 base (such as n-butyllithium in hexanes) in a solvent (such as tetrahydrofuran), (such as tetrakis(triphenylphosphine)palladium(0)) to yield sulfonamide 6. carbonate), a benzyl halide (such as p-methoxybenzyl chloride), and a catalyst (ii) an electrophile (such as trimethyl borate), and (iii) a base (such as sodium Treatment of sulfonamide 6 with a fluoride source, such as
- 8 5 R\* and q are as previously defined above for compounds of Formula I. tetrabutylammonium fluoride, in a solvent, such as tetrahydrofuran, provides oxidized using a method such as Swern Oxidation to yield sulfonamide the deprotected sulfonamide alcohol 7. Sulfonamide alcohol 7 is successively aldehyde 8 is converted to racemic benzothiazepines 9a and 9b. R1, R2, R3, RN aldehyde 8. Upon treatment with a base such as potassium tert-butoxide,

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SCHEME 2

Alternative Synthesis of sulfonamide alcohol

5 1. R', R2, R\* and q are as previously defined above for compounds of Formula benzenesulfonamide 3 which can be further reacted in accordance with Scheme I. Substituent M is a metal, preferably an alkali metal, or a hydrogen. base, such as triethylamine, in a solvent, such as tetrahydrofuran, yields Reaction of sulfonamide 12 with a suitable nucleophile in the presence of a as fluoro, chloro, bromo, nitro, tosyloxy or trifluoromethylsulfonyloxy. Substituent L of benzenesulfonyl chloride 10 is a suitable leaving group such triethylamine, in a solvent, such as tetrahydrofuran, yields sulfonamide 12. chloride 10 with aminoalcohol 11 in the presence of a base, such as of sulfonamide alcohol 3 used in Scheme 1. Reaction of benzenesulfonyl Scheme 2 illustrates an alternative synthetic scheme for the preparation

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Scheme 3 illustrates the preparation of benzothiazepines having 4-position substituents other than hydroxy.

position substituents other than hydroxy.

In the preparation of 4-thioxo-, thio-, sulfinyl- or sulfonylbenzothiazepines, benzothiazepine 9a or 9b is first oxidized to
benzothiazepine-4-one 13. Conventional oxidizing agents, such as PCC, or
Swern conditions can be used. Benzothiazepine-4-one 13 is then reacted with
Lawesson's Reagent to produce 4-thioxo-benzothiazepine 14. 4-Thioxobenzothiazepine 14 can be reacted with a suitable reducing agent, such as
lithium aluminum hydride, in a suitable solvent, such as tetrahydrofuran, to

yield 4-mercapto-benzothiazepine 15. 4-Mercapto-benzothiazepine 15 can be reacted with a suitable alkylating agent, such as an alkyl halide, in the presence of a base, such as sodium bydride, in a suitable solvent, such as dimethylformamide, to yield 4-alkylthio-benzothiazepine 16. 4-Alkylthio-benzothiazepine 16 can be reacted with a suitable oxidizing agent, such as butyl hydroperoxide or m-chloroperbenzoic acid, to yield, successively, 4-alkylsulfinyl-benzothiepine 17 and 4-alkylsulfonyl-benzothiazepine 18.

Alternatively, 4-amino- or imino-benzothiazepines can be prepared by reacting benzothiazepine-4-one 13 with ammonia or a primary amine in a suitable solvent, such as tetrahydrofuran, to produce 4-imino-benzothiazepine

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19. 4-Imino-benzothiazepine 19 can be reacted with a suitable reducing agent, such as lithium aluminum hydride, in a suitable solvent, such as tetrahydrofuran, to yield 4-amino-benzothiazepine 20. Benzothiazepine-4-one 13 also can undergo reductive alkylation by reaction with ammonia, a primary amine or a secondary amine in the presence of an reducing agent, such as sodium triacetoxyborohydride, in a suitable solvent, such as tetrahydrofuran, to

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produce 4-amino-benzothiazepine 21.

Scheme 3 also illustrates the preparation of 4-alkyl-benzothiazepine 23 and 4-alkoxycarbonyl-benzothiazepine 25. The 4-position hydroxy of benzothiazepine 99 or 9b is first converted to a suitable leaving group such as mesyloxy to form protected benzothiazepine 22. Protected benzothiazepine 22.

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is then reacted with a suitable nucleophile, such as butyl lithium, in a suitable solvent, such as tetrahydrofuran, to yield 4-alkyl-benzothiazepine 23.

Alternatively, protected benzothiazepine 22 can be reacted with a suitable cyanidating agent, such as an potassium cyanide, in a suitable solvent, such as dimethylformamide, to yield 4-cyano-benzothiazepine 24. 4-Cyano-benzothiazepine 24 is converted to 4-alkoxycarbonyl-benzothiazepine 25 by reaction with a suitable alcohol in the presence of a base, such as potassium hydroxide.

The recovery, isolation and purification of the intermediates and the reaction products of this invention, and in particular the intermediates and the reaction products illustrated in Schemes 1, 2, 3 and 4, can be accomplished by conventional methods well known to those skilled in the art, such as

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precipitation, filtration, extraction, or chromatography. Except where otherwise indicated, conditions, solvents, and reagents are either conventional, not narrowly critical, or both.

## Additional Embodiments and Examples

example, alkylcarbonyl, alkoxy, hydroxy, and nitrogen-containing heterocyclyl include ethyl, n-propyl, n-butyl, n-pentyl, isobutyl, isopropyl, -CH<sub>2</sub>C(=0)C<sub>2</sub>H<sub>3</sub>, joined to the C.10 alkyl through an ether linkage. These R' and R2 substituents invention, substituents R' and R2 are identical, for example n-buty/n-butyl, so -CH<sub>2</sub>OC<sub>2</sub>H<sub>3</sub>, and -CH<sub>2</sub> O-(4-picoline). Ethyl, n-propyl, n-butyl, and isobutyl that the compound is achiral at the 3-position carbon. Eliminating optical are preferred. In certain particularly preferred compounds of the present separation, and quality control of the compound used as an ileal bile acid Another class of compounds of specific interest comprises those comprises one or more radicals independently selected from among, for substituted and unsubstituted C1.10 alkyl wherein substituted C1.10 alkyl isomerism at the 3-position carbon simplifies the selection, synthesis, compounds of Formula I wherein R1 and R2 are selected from among transport inhibitor. 2 2

In the compounds of the present invention having a chiral 3-position carbon as well as those having an actiral 3-position carbon as well as those having an actiral 3-position carbon, substituents R\* on the benzo ring can include, for example, hydrogen, aryl, alkyl, hydroxy, halo, alkoxy, alkylstulfinyl, alkylsulfinyl, haloalkyl, haloalkyl, haloalkox, (M)-hydroxy-carbonylalkylamino, haloalkylthio, haloalkylsulfinyl, haloalkylsufonyl, amino, N-alkylamino, N,N-dialkylamino, (M)-3 alkoxycarbamoyl, (M)-aryloxycarbamoyl, (N)-aralkyloxycarbamoyl,

alkoxycarbamoyl, (N)-aryloxycarbamoyl, (N)-aralkyloxycarbamoyl, trialkylammonium (especially with a halide counterion), (N)-amido, (N)-alkylamido, (N)-haloalkylamido, (N)-sulfonamido, (N)-sulfonamido, (N)-haloalkylsulfonamido, carboxyalkylamino, trialkylammonium salt, (N)-carbamic acid, alkyl or benzyl ester, N-acylamino

a halo or a quaternary ammonium salt, and (N)-nitrogen containing salt substituted thereon, -[O(CH2)<sub>d</sub>]<sub>e</sub>-X where e is 2 to 12, d is 2 or 3 and X is of the alkyl substituents, an alkylene bridge having a quaternary ammonium ammonium salt having a carboxylic acid or hydroxy substituent on one or more heterocyclyl wherein the nitrogen of said heterocyclyl is optionally hydroxylamino, haloacylamino, carbohydrate residue, thiophene, a trialkyl

bromo, fluoro, methylsulfinyl, methylsulfonyl, ethylthio, amino, isopropyl, t-butyl, hydroxy, methoxy, ethoxy, isopropoxy, methylthio, iodo, Among the preferred species which may constitute R\* are methyl, ethyl,

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t-butyloxycarbamoyl, (N)-methylsulfonamido, (N)N-methylpyrrolidinium, and N+(CH<sub>3</sub>)<sub>2</sub> CO<sub>2</sub> H I; -NCH<sub>3</sub> CH<sub>2</sub> CO<sub>2</sub>H, -(N)-N'-dimethylpiperazinium I; (N)methylpiperazinyl, (N)-bromomethylamido, (N)-N-hexylamino, thiophene, methylpyridinium A-, (N)-N-methylmorpholinium A-, and N-N'hydroxylamino, N-methylamino, N,N-dimethylamino, N,N-diethylamino, (N)azetidinyl, (N)-N-methylazetidinium A-, (N)-pyrrolidinyl, pyrrolyl, (N)-N-NHC(=0)C<sub>3</sub>H<sub>11</sub>, -NHC(=0)C<sub>6</sub>H<sub>13</sub>, carboxyethylamino, (N)-morpholinyl, (N)benzyloxycarbamoyl, trimethylammonium A; -NHC(=0)CH3,

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residue (e.g., a 5 or 6 carbon monosaccharide residue), peptide residue, and e.g., -(OCH<sub>2</sub> CH<sub>2</sub>)<sub>k</sub> -N+R <sup>13</sup>R <sup>14</sup>R <sup>15</sup>A; where x is 2 to 10 quaternary ammonium salts linked to the ring via poly(oxyalkylene) linkages the benzo ring including, for example, guanidinyl, cycloalkyl, carbohydrate substituents can be advantageously present on the 6, 7, 8, and/or 9- positions of compounds, for example the 6,7,8-trimethoxy compounds. A variety of other disubstituted at the 7- and -8 positions. Also included are the 6,7,8-trialkoxy The benzo ring can be mono-substituted at the 6, 7 or 8 position, or

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-(OCH2CH2)31, where A: is a pharmaceutically acceptable anion

unsubstituted aryl, thiopene, pyridine, pyrrole, thiazole, imidazole, pyrazole independently selected from among hydrogen and ring-carbon substituted or In further compounds of the present invention, R5 and R6 are

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(0,0)-dioxyalkylene, -[0(CH<sub>2</sub>)<sub>d</sub>]<sub>e</sub>X where e is 2 to 12, d is 2 or 3 and x alkoxycarbonyl, aryloxycarbonyl, alkylcarbonyloxy and arylcarbonyloxy alkylene bridge having a quaternary ammonium salt substituted thereon, alkylamino, N,N-dialkylamino, quaternary ammonium salts, a C, to C. comprises halo or a quaternary ammonium salt, thiophene, pyridine, pyrrole, among, for example, halo, hydroxyl, trihaloalkyl, alkoxy, amino, Nalkylmorpholinium, or furan in which the substituent(s) are selected from pyrimidine, morpholine, N-alkylpyridinium, N-alkylpiperazinium, N-

substituted, or di-substituted. phenyl, phenylene, or benzene triyl, i.e., may be unsubstituted, mono-Among the species that may constitute the substituents on the aryl ring

thiazole, imidazole, pyrazole, or furan. The aryl group of R3 or R6 is preferably

5

of R5 or R6 are fluoro, chloro, bromo, methoxy, ethoxy, isopropoxy, trimethylammonium (preferably with an iodide or chloride counterion)

- 15 Other substituents that can be present on a phenylene, benzene triyl or other each substituted at the p-position, the m-position, or both of the aryl ring. tri(oxyethylene)iodide, and tetra(oxyethylene)trimethyl-ammonium iodide, methoxycarbonyl, ethoxycarbonyl, formyl, acetyl, propanoyl, (N)hexyldimethylammonium, hexylenetrimethylammonium
- 20 methoxyphenyl, p-N,N-dimethylaminophenyl, m-N, N-dimethylaminophenyl, fluorophenyl, p-hydroxyphenyl, m-hydroxyphenyl, p-methoxyphenyl, mthose in which R' or R' is selected from phenyl, p-fluorophenyl, mdioxyethylene (6-membered ring). One group of compounds of interest are aromatic ring includes 3, 4-dioxymethylene (5-membered ring) and 3, 4-
- 30 25 (N,N-dimethylpiperazinium)+(N')-CH<sub>2</sub>-OCH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>-O-phenyl, 3-fluoro-4fluorophenyl, thienyl-2-yl, 5-cholorothienyl-2-yl, 3, 4-difluorophenyl, I-p-(N,N-dimethylpiperazinium)-(N')-CH<sub>2</sub>-(OCH<sub>2</sub>CH<sub>2</sub>),-O-phenyl, 3-methoxy-4 I' p-(CH<sub>3</sub>)<sub>3</sub>-N\*-phenyl, I' m-(CH<sub>3</sub>)<sub>3</sub>-N\*-phenyl, I' m-(CH<sub>3</sub>)<sub>3</sub>-N\*-CH<sub>2</sub>CH<sub>2</sub>-(OCH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>-O-phenyl, I' p-(CH<sub>3</sub>)<sub>3</sub>-N<sup>+</sup>-CH<sub>2</sub>CH<sub>2</sub>-(OCH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>-O-phenyl, I' m-
- methoxyphenyl, 4-pyridinyl, 2-pyridinyl, 3-pyridinyl, N-methyl-4-pyridinium

I. N-methyl-3-pyridinium, 3, 4-dioxymethylenephenyl, 3, 4dioxyethylenephenyl, and p-methoxycarbonylphenyl.

compounds having each of the above preferred R3 substituents in combination with the R\* substituents shown in Tables 1, 2 and 3 below. It is particularly Preferred compounds include 3-ethyl-3-butyl and 3-butyl-3-butyl preferred that one, but not both, of R5 and R6 is hydrogen.

be hydrogen, and that R3 and R3 be oriented in the same direction relative to the It is especially preferred that R' and R' be hydrogen, that R' and R' not plane of the molecule, i.e., both in a. or both in \theta-configuration. It is further preferred that, where R2 is butyl and R1 is ethyl, then R1 has the same

orientation relative to the plane of the molecule as R3 and R3.

2

second part of Table 1 identifies the R\* radical or radicals for those compounds. Table 1 identifies the R1, R2, R3, R4 and R5 radicals for each compound and the benzothiazepines wherein the R1, R2, R3 and R3 radicals are as set forth in Table 1 below; the R6 radical is hydrogen; the RN radical is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, n-butyl, n-pentyl, nfrom the group of R' radicals disclosed in Table 1 below. The first part of hexyl and benzyl; and the R\* radical or radicals are independently selected A class of compounds of particular interest comprises those 1,2-

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4-(decyloxy)phenyl phenyl 4-(decyloxy)phenyl phenyl u-pntλ|
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> (K<sub>x</sub>)<sup>d</sup> Ig mm

> > TABLE 1

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110	ethyl	n-butyl	OH	Н	phenyi
111	n-butyl	ethyl	ОН	Н	
112	ethyl	n-butyl	OH	H	4-hydroxyphenyl O S N H <sub>2</sub> N  H <sub>2</sub> N  H <sub>3</sub> N  H <sub>3</sub> N  H <sub>4</sub> N  H <sub>5</sub> N  H <sub>5</sub> N  H <sub>6</sub> N  H <sub>7</sub> N  H <sub>7</sub> N  H <sub>8</sub> N  H
	ethyl	n-butyl	OH	Н	4-hydroxyphenyl
	ethyl	n-butyl	ОН	H	4-methoxyphenyl
	r-butyl	ethyl	OH	Н	4-methoxyphenyl
	ethyl	n-butyl	ОН	н	4-methoxyphenyl
	ı-butyl	ethyl	ОН	H	phenyl
	ethyl	n-butyl	ОН	H	phenyl
	ethyl	n-butyl	OH	H	phenyl
	-butyl	ethyl	ОН	H	phenyl
	ethyl	n-butyl	OH ·	н	phenyl
	-butyl	ethyl	OH	н	phenyl
123	ethyl	n-butyl	OH	н	phenyl

	phenyl	H	OH	ethyl	n-butyl	124
	phenyl	н	ОН	n-buty!	ethyl	125
	4-fluorophenyl	н	OH	ethyl	n-butyl	126
	4-fluorophenyl	н	ОН	ethyl	n-butyl	127
	4-fluorophenyl	H	OH	n-butyl	ethyl	128
	4-fluorophenyl	н	ОН	n-butyl	ethyl	129
	4-fluorophenyl	н	OH	n-butyl	ethyl	131
	phenyl	H	ОН	n-butyl	ethyl	132
	phenyi	H	OH	n-butyl	ethyl	133
	phenyl	H	ОН	n-butyl	ethyl	134
	phenyl	H	OH	n-butyl	ethyl	135
	phenyl	Н	ОН	n-butyl	ethyl	136
	phenyl	Н	· OH	ethyl	n-butyl	137
	phenyl	Н	OH	ethyl	n-butyl	138
	Phenyi	Н	OH	ethyl	n-butyl	139
	Н	OH	H	n-butyl	ethyl	142
	3-methoxyphenyl	н	ОН	n-butyl	ethy!	143
	4-fluorophenyl	H	OH	n-butyl	ethyl	144
	3-methoxyphenyl	н	OH	n-butyl	ethyl	262
	Н	OH	Н	n-butyl	ethyl	263
	3-trifluoromethylphenyl	н	ОН	n-butyl	ethyl	264
	Н	OH	Н	n-butyl	ethyl	265
	3-hydroxyphenyl	н	OH	n-butyl	ethyi	266
	3-bydroxyphenyl	H	OH	n-butyl	ethyl	267
	4-fluorophenyl	Ĥ	OH	n-butyl	ethyl	268
	Н	OH	H	n-butyl	ethyl	269
———	4-fluorophenyl	Н	OH	n-butyl	ethyl	270
	3-methoxyphenyl	н	OH	n-butyl	ethyl	271
	Н	ОН	Н	n-butyl	ethyl	272
	H	OH	Н	n-butyl	ethyl	273
	4-fluorophenyl	н	ОН	n-butyl	ethyl	274
	Н	OH	н	n-butyl	ethyl	275
	3-methoxyphenyl	н	OH ·	n-butyl	ethyl	276

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	н	но	r-pniyi	сџуј	<b>56</b> Z
репу	н	но	lýmo-n	I-butyl	767
репу	H	но	ı/inq-u	[Ang-u	767
4-Пиоторьсту!	H	HO	I/Jud-a	n-butyl	767
penyl	H	НО	1/ting-a	r-pnr/s	162
ріспу	н	но	n-path]	n-butyl	067
русиу	H	но	p-pntyl	n-pntλj	68Z
русиу	н	но	methyl	ισετρλι	788
Бусилі	H	но	сгруј	сруј	<u> </u>
руслуј	Н	но	сцрλј	crph	286
-fluotophenyl	Н	но	n-butyl	ethyl	787
Н .	НО	н	a-butyl	сфуј	283
4-fluorophenyl	H	но	a-butyl	сџѝј	282
ф-Пиоторьскуї	H	НО	n-butyl	ethyl	182
устористу С	Н	но	lytud-a	cthyl	087
lynadgorouf)-E	HO	H	n-butyl	cthyl	642
Z-fluorophenyl	но	H	a-butyl	ςφλ]	872
lynorophenyl	Н	но	lytud-n	сгруі	LLZ

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1004	ethyl	n-butyl	ОН	н	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \
					CF <sub>3</sub> COO- + (CH <sub>3</sub> CH <sub>2</sub> ) <sub>3</sub> N
1005	n-butyl	n-butyl	OH	н	CF <sub>3</sub> COO- (CH <sub>3</sub> CH <sub>2</sub> ) <sub>3</sub> N
1006	n-butyl	n-butyl	ОН	Н	F N Br-

1007	n-butyl	n-butyi	ÖН	н	<u> </u>
					+ I- N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub>
1008	n-butyl	n-butyl	ОН	н	
					$\perp$
	·				
1009	n-butyl	n-butyl	OH	Н	
					1-  -  -  -  -  -  -  -  -  -  -  -  -  -
1010	n-butyl	n-butyl	ОН	Н	3-fluoro-4-methoxyphenyl
1011	n-butyl	n-butyl	OH	H	3-fluoro-4-(5-triethylammoniumpentyloxy)phenyl, trifluoroacetate salt
1012	n-butyl	n-butyl	OH	H	4-hydroxyphenyl

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	н	но	n-patyl	n-patyl	9101
Br. Br.	н	но	u-pn;λ,	u-pnţλ <u>ı</u>	SIOI
φ-methoxyphenyl	н	но	n-path	u-prtyl	1014
0 + (CH <sup>3</sup> ) <sup>3</sup> + 1-					
	Н	но	n-pntλj	υ-ρπέλι	1013

1019	n-butyl	n-butyl	ОН	н	CF <sub>3</sub> CO <sub>T</sub> (CH <sub>2</sub> ) <sub>4</sub> (CH <sub>2</sub> ) <sub>4</sub> (CH <sub>2</sub> ) <sub>4</sub>
1020	n-butyl	n-butyl	ОН	Н	CI- N(CH <sub>2</sub> CH <sub>3</sub> )
1021	n-butyl	n-butyl	ОН	Н	I- OH OH

1022	n-butyl	n-butyl	ОН	н	I- OH
1023	n-butyl	n-butyl	OH	H	

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92	+ N -1 O	н		į⁄unq-a		
	+ 1		но		JAmq-u	
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	N(CHFCHP)	н	но	[Ænq-u	[Kinq-u	5201
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1029	n-butyl	n-butyl	ОН	Н	
					1.
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1030	n-butyl	n-butyl	ОН	н	l J <sub>3</sub>
	1		]	<u> </u>	
			[		I- N
				[	+
1031	n-butyl	n-butyl	ОН	н	1 J <sub>3</sub>
					CF <sub>3</sub> CO <sub>2</sub>
			[		(CH <sub>2</sub> ) <sub>4</sub> (CH <sub>2</sub> ) <sub>4</sub>
					O O N(CH₂CH₃)
1					·

1032	n-butyl	n-butyl	ОН	н .	CF <sub>3</sub> CO <sub>2</sub> + N(CH <sub>2</sub> CH <sub>3</sub> )
1033	n-butyl	n-butyl	OH	H	F N Br-

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-1	н	но	lyind-n	lyiud-a	1034

1038	n-butyl	n-butyl	OH	н	I- + N(CH <sub>3</sub> ) <sub>3</sub>
1039	n-butyl	n-butyl	OH	н	phenyl
1040	n-butyl	n-butyl	OH	Н	F CF <sub>3</sub> CO <sub>2</sub> (CH <sub>2</sub> ) <sub>4</sub> (CH <sub>2</sub> ) <sub>4</sub> N(CH <sub>2</sub> CH <sub>3</sub> ) +
1041	n-butyl	в-butyl	ОН	Н	I- N + N + N + N + N + N + N + N + N + N

				•	
1042	n-butyl	n-butyl	ОН	н	I- + N(C <sub>6</sub> H <sub>5</sub> )
1043	n-butyl	n-butyl	ОН	н	
1044	n-butyl	n-butyl	OH	Н	F CF <sub>3</sub> CO <sub>2</sub> + N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub>
1045	n-butyl	n-butyl	ОН	Н	F CF <sub>3</sub> CO <sub>2</sub> - (CH <sub>2</sub> ) <sub>8</sub> + N(CH <sub>2</sub> CH <sub>3</sub> )
1046	n-butyl	n-butyl	ОН	н	3-aminophenyl

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001	CE <sup>3</sup> CO <sup>3</sup>	н	но	j£inq−a	<b>μέλεια-α</b>	1501
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	<del> </del>		HU	lvindin	lvtud-n	1050

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44	Br. Br.	н	но	լՀյոզ-ս	l/Sinq-u	6701
	O + (CH <sup>3</sup> CH <sup>3</sup> ) <sup>3</sup>	н	но	[Ainq-u	n-pntyl	1048
	I- N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub>					
	<u> </u>	н	но	n-butyl	ր/փոզ-ա	<b>∠</b> ₩01

1053	n-butyl	n-butyl	ОН	н	CF <sub>3</sub> CO <sub>2</sub> (CH <sub>2</sub> ) <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub>
1054	n-butyl	n-butyl	ОН	Н .	1- 1- N+ N+

1055	n-butyl	n-butyl	ОН	Н	
	n-butyi	n-outyi	ОН	н	I- N N
1056	n-butyl	n-butyl	ЮН	Н	1- N+ + + + + + + + + + + + + + + + + + +
1057	n-butyl	n-butyl	ОН	Н	1

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		н	но	ո-բուչվ	υ-ρηέλι	1901
ŀ	3-fluoto-4-methoxyphenyl	н	но	n-butyl	сфуј	1000
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	´ ł <u>`</u>	н	но	n-butyl	n-butyl	8501

1064	n-butyl	n-butyl	OH	Н	
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1065	n-butyl	n-butyl	ОН	, n	
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					N(((CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> CH <sub>3</sub> )
_			<u> </u>	ļ	l J <sub>3</sub>

1066	n-butyl	n-butyl	OH	н	r- ,
1067	n-butyl	n-butyl	ОН	Н	thiophen-3-yl
1068	n-butyl	n-butyl	ОН	H	<u> </u>
1069	n-butyl	n-butyl	OH	H	phenyl
1070	n-butyl	n-butyl	ОН	Н	F CF <sub>3</sub> CO <sub>2</sub> + N

4-bydroxypbenyl	Н	но	յ/մաժ-ո	ειμλι	8/01
3-һуфохуласфуфепуі	н	но	lyiud-a	[\timed-ra	LLOI
1- + N(CH <sub>3</sub> ) <sub>3</sub>	н	но	ivind-a	l∀iva-a	9401
4-Duorophenyl	H	но	į/inq-ti	[ʎɪnq-u	SLOI
3-fluoro-4-methoxyphenyl	Н	НО	n-butyl	esphl	<b>PL01</b>
	н	но	park) i	u-pniyl	£401

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107						
	-1	н	но	o-pnikj	ր-թուհլ	1401

ethyl n-butyl OH H		
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ı	1080	n-butyl	n-butyl	ОН	Н	<u> </u>
		li:				
	1081	n-butyl	n-butyl	OH	Н	
	-			-		1- O O O O O O O O O O O O O O O O O O O
	1082	n-butyl	n-butyl	OH	Н	2-pyridyl
	1083	n-butyl	n-butyl	ОН	H	1- 0 1- 1-

112	-1 -1	Н	но	Į∕unq-u	į King-u	1601
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<b>←шс</b> фохурьспу!	н	но	I/smq-ti	ctbyl	6801
3,4-methylenedioxyphenyl	Н	НО	JAnq-u	сгруг	8801
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ly-E-madoidt	H	HO	n-butyl a-butyl	υ-ραιλ <u>ι</u>	9801 9801
+ + O					
	н	но	Içind-a	n-pntyl	1084

1092	n-butyl	n-butyl	ОН	н	
1093	n-butyl	n-buty!	ОН	Н	
. 1094	n-butyl	n-butyl	ОН	Н	1- 1- 1- 3

1095	n-butyl	n-butyl	ОН	н	
1096	n-butyl	n-butyl	OH	Н	1- 0 - 1- 3
1097	n-butyl	a-butyi	ОН	н	O Br

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		н	но	u-pni31	u-pngAj	6011
_ h	lybinyq-E	Н	но	a-butyl	n-butyl	1108
116	Br + +			_		
ı i.	•	н	но	n-butyl	a-butyl	7011
Г	2-ріресову! 3-ріфсову!	H	HO.	IYind-a	n-butyl	9011
Г	5-piperoxyl	Н	но	ա-թումկ	I\taud-a	5011
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3-сягрох/ансцу/фуспу]	Ĥ	но	n-bury!	u-pntyl	2011
t cErcor.	н	но	<b>ս</b> -բուչկ	ерпуу	1011
4-methoxyphenyl	н	но	Ivind-a	a-pntyl	1100
ф-шегрохурусаў [	н	НО	p-pntyl	сфуј	6601
O (CH <sup>3</sup> CH <sup>3</sup> ) <sup>3</sup> R (CH <sup>3</sup> CH <sup>3</sup> ) <sup>3</sup> 1-	н	но	p-pntλj	ı Çınç-u	8601

1110	n-butyl	n-butyl	ОН	Н	1- N-
	n-butyl	n-butyl	ОН	H	CF <sub>3</sub> CO <sub>2</sub>
1112	n-butyl	n-butyl	ОН	н	4-pyridyl
1113	n-butyi	n-butyl	ОН	Н	F o o
1114	n-butyl	n-butyl	OH	н	3-methoxyphenyl
1115	n-butyl	n-butyl	OH	H	4-fluorophenyl
1116	ethyl	n-butyl	OH	Н	3-tolyl

1117	ethyl	n-butyl	ОН	н	I- + N(CH <sub>3</sub> )
1118	ethyl	n-butyl	OH	H	3-fluoro-4-hydroxyphenyl
1119	n-butyi	n-butyl	OH		1- 1- N+ N+ N+ N+ N+ N+ N+ N+ N+ N+ N+ N+ N+
1120	n-butyl	n-butyl	ОН	Н	1- + 0 3

ф-сумотету/ррепу!	Н	НО	lytud-a	a-butyl	EELL
<u> </u>	н	но	n-pm;	ι/ςιης-τι	7511
ф-инсарохуррспу ј	н	но	u-preyl	сцууј	1131
3-chloro-4-fluorophenyl	Н	HO	n-butyl	I-činā-a	1130
ф-Пиоторьску!	н	HO	lyjud-a	p-prtyl	6711
3-Ωποτηγραμετιγή	н	но	n-prityl	u-prtλį	8711
+N -1 -1	н	но	l⁄zud-n	Į.Kīnq-u	<b>4211</b>

					1176
3-chloxyabenyl					5711
3-methoxynhenyl					1124
lumda 1	п		hend-o	panqu	1123
Br N(CHFCHP)	н	но	p.King-u	j.Kinq-a	7211
	3-celoro-4-methoxyphemyl  3-methoxyphemyl  phemyl  A(CH2CH3)	H 3-ciplor-4-methoxyphenyl  H 3-ciplor-4-methoxyphenyl  H 5-ciplor-4-methoxyphenyl  H Br  H (CH <sup>2</sup> CH <sup>3</sup> )	OH H 3-cplous-4-methoxyphemyl OH H 3-methoxyphemyl OH H 3-methoxyphemyl OH H 5-methoxyphemyl OH H 10-methoxyphemyl OH H 3-methoxyphemyl	α-ρπλη         OH         H         3-ciplora-4-απειροχλήριεση 1           α-ρπλη         OH         H         3-ciplora-4-απειροχλήριεση 1           α-ρπλη         OH         H         β-cmλη           α-ρπλη         OH         H         β-cmλη           α-ρπλη         OH         H         M(CH <sup>2</sup> CH <sup>3</sup> )	ετριλι         υ-ρπιλι         OH         H         3-cυριου-4-σεσροχλόρεσλι           υ-ρπιλι         OH         H         3-cυριου-4-σεσροχλόρεσλι           υ-ρπιλι         OH         H         3-cυριου-4-σεσροχλόρεσλι           υ-ρπιλι         OH         H         Dycσλι           υ-ρπιλι         OH         H         Dycσλι

1134	ethyl	n-butyl	OH	Н	· \
1135	n-butyl	n-butyl	OH	н	3,4-dimethoxyphenyl
1136	n-butyl	n-butyl	OH	н	
1137	n-butyl	n-butyl	OH	н	4-fluorophenyl
1138	n-butyl	n-butyl	ОН	Н	1- N+ +
1139	n-butyl	n-butyl	OH	н	3,4-difluorophenyl
1140	n-butyl	n-butyl	OH	н	3-methoxyphenyl

1141	n-butyl	p-butyl	OH	Н	4-fluorophenyl
1142	n-butyl	n-butyl	ОН	Н	F N(CH <sub>2</sub> CH <sub>3</sub> )
1143	n-butyl	n-butyl	н	OH	Н
1144	n-butyl	n-butyl	ОН	Н	5-piperonyl
1145	n-butyl	n-butyl	OH	Н	4-methoxyphenyl
1146	n-butyl	n-butyl	OH	Н	I (CH <sub>2</sub> ) <sub>1Q</sub> N(CH <sub>3</sub> ) <sub>3</sub> +
1147	n-butyl	n-butyl	OH	H	
1148	n-butyl	n-butyl	OH	Н	4-fluorophenyl
1149	n-butyl	n-butyl	ОН	Н	4-fluorophenyl
1150	n-butyl	n-butyl	OH	Н	3-methoxyphenyl
1151	n-butyl	ethyl	ОН	Н	3-fluoro-4-methoxyphenyl
1152	n-butyl	n-butyl	OH	Н	phenyl
1153	n-butyl	n-butyl	OH	н	4-fluorophenyl
1154	n-butyl	n-butyl	OH	Н	3-methoxyphenyl
1155	n-butyl	n-butyl	ОН	Н	4-fluorophenyl
1156	n-butyl	n-butyl	OH	Н	4-fluorophenyl
1157	n-butyl	n-butyl	OH	Н	4-fluorophenyl
1158	n-butyl	n-butyl	OH	Н	4-pyridinyl, hydrochloride salt
1159	n-butyl	ethyl	OH	н	phenyl
1160	n-butyl	n-butyl	OH	H	4-fluorophenyl

4-тейохуриспу	H	НО	lytud-n	n-butyl	5611
HO					
4-(2-(2-mcthylpropyl))phenyl	H H	HO	lyind-a lyind-a	lybud-m lybud-m	<b>7611</b>
3-(dimethylamino)phenyl	н	HO	n-butyl	lytud-a .	£611
4-(dimethylamino)phenyl	H	HO	Ivind-a	lçind-a	7611 1611
Z-bromophenyl	H	HO	[thuc-n	n-butyl	0611
lynadroroudib-b,£	H	HO	n-butyl	a-butyl	6811
honed-month h f	n	nO n	heaved a	leaved a	0811

ф-тегрохурьеву!	н	НО	n-prityl	n-pntyl	1188
ү-(уголобуса)	н	но	I-butyl	1/21mq-12	4811
δρευλι	Н	НО	I/(Inq-u	n-butyl	9811
4-fluorophenyl	н	НО	Ivina-a	u-prekj	5811
4-Пиогорьспу	н	но	I-butyl	n-pntyl	1184
3-тетрохурічету [	H	но	n-butyl	n-pntyl	1183
4-(dimethylamino)phenyl	H	HO	B-pntyl	l/ind-a	1182
[γε⊃ήqσιομΩ>	Н	но	n-parki	n-pntyl	1181
репу	H	но	I/Jang-u	Içind-ri	0811
bpcnNf	H	но	η/snq-α	I-butyl	6/11
3-(trifluoromethylsulfonyloxy)phenyl	H	но	lyind-a	L(110-ti	
3-шефохуруену [	H	но	l/ing-a	a-buryl	11.18 14.11
4-Пиоторіленуї	H	но	D-pritkj	[Ang-u	
3-тастохурнату!	H	но	Içtud-a	crphj	9/11 S/11
3-тегрохуристу!	H	HO	n-butyl	cayl	7/11
4-циохоруси) г	H	но	n-prit)	n-buryl	
- pyridiny!	H	но	n-butyl	n-butyl	2711
4-(trifinoromethylaulfonyloxy)phenyl	H	но	Iking-u	n-butyl	1/11
3-тегрохурьсту!	Ĥ	но	[Amq-u	n-busyl	0/11
ppcnyl	Н	но	King-u	a-buryl	6911
ф-руспохурьелу!	-  <del>''</del> H	но.	n-butyl	lyind-a	8911
CI	н	но	Į∕smq-u	J&inq-a	<b>4911</b>
3-руфгохурьсту!	н	но	υ-ρατλι	Içind-a	9911
3-thoro-4-methoxyphenyl	H	но	u-prik	l/thd-a	5911
lymbtryq-≯	н	но	u-prikl	a-parki	9911
3-(dimethylamino)phenyl	H	но	u-pntλj	D-pathy	
bycon	H	HO	1/2110-0	D-partyl	1163
3,5-dichloro-4-methoxyphenyl		ן אט		luttidan	1162

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1196	n-butyl	n-butyl	OH	н	I + N(CH3)
1197	n-butyl	ethyl	R3 + R4 = oxo	R3 + R4 = oxo	phenyl
1198	n-butyl	n-butyl	OH	Н	4-(pyridinyl-N-oxide)

OH H

H

n-butyl n-butyl

n-butyl

n-butyl n-butyl

1200 1201

4-тегрохуррету!	н	НО	I\(\tau\)	I-butyl	1218
4-carboxyphenyl	Н	НО	n-butyl	I\71ud-n	LIZI
lynorapiq-2	H	но	n-butyl	cthyl	9171
4-тесфохуррспу1	H	НО	P(t)nd-a	n-butyl	1512
ppcoyl	Н	но	cthyl	[⟨tinq-α	1514
	но	н	ετρλη	1/110d-rs	1213
4-methoxyphenyi	н	НО	p-butyl	n-butyl	1717
DOH E					
· · · · · · · · · · · · · · · · · · ·	н	но	ը/փոզ-ա	ετρλη	1171

у-(-(diracthylamino)рhenyl	н	но	n-press	ı/mq-u	1210
phenyl	H	acetoxy	n-butyl	n-butyl	1210
4-methoxyphenyl	Н	НО	D-butyl	I-butyl	8021
3,5-dichlorophenyl	н	но	lytud-a	JAmq-u	1207
N(CH <sup>3</sup> CH <sup>3</sup> )			ă. ₽		
B	н	но	iVind-a	lyjud-n	9071
	н	но	Į∕sinq-u	γένια- <del>υ</del>	15051
4-iluotophenyl	Н	но	n-butyl	ivind-a	1504
λίψεταςψό-ς	H	HO	n-butyl	n-pntyl	1203
1 (CH <sup>3</sup> ) <sup>3</sup>					
	н	но	į£iną-u	n-butyl	70 <b>7</b> 1

N(CH <sub>3</sub> )	н	ОН	n-butyl	n-butyl	1219
~ `0' ~					
3-methoxyphenyl	H	ОН	n-butyl	n-butyl	1220
CO <sub>2</sub> CH <sub>3</sub>	Н	ОН	a-butyl	n-butyl	1221
 3-methoxyphenyl	H	OH	n-butyl	n-butyl	1222
 phenyl	Н	OH	n-butyl	n-butyl	1223
 3-nitrophenyl	H	OH	n-butyl	n-butyl	1224
 3-methylphenyl	H	OH	ethyl	n-butyl	1225
 5-piperonyl	н	OH	n-butyl	ethyl	1226
 4-fluorophenyl	H	OH	n-butyl	n-butyl	1227
 2-pyrrolyl	н	OH	n-butyl	n-butyl	1228
 3-chloro-4-hydroxyphenyl	н	ОН	n-butyl	n-butyl	1229
 phenyl	н	ОН	n-butyl	n-butyl	1230

1231	n-butyl	n-butyl	OH	н	7
	-				
1232	n-butyl	n-butyl	Н	OH	3-thiophenyl
1233	n-butyl	n-butyl	OH	H	Br N(CH <sub>3</sub> )
1234	n-butyl	n-butyl	он	н	Br + N(CH <sub>3</sub> )

N(CH³)	1				·
+					
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/   \	н	но	l/ind-a	Ivind-a	1542
3-тетрохурдепу!	H	НО	n-butyl	lytud-n	1544
, HO			Ì	<b>i</b> .	
1 1				Ī	
(cH <sub>3</sub> )N.				İ	
1 \ / / /		1	_	_	
+ 🗸 🗸 🔼	н	НО	lytud-a	lytud-a	1543
<b>*</b> [ ]			•	J	
104 ~ 1			]	ļ	
	1				
3 (	H	HO HO	n-butyl a-butyl	n-butyl	1545 1541
4-methoxy-3-methylphenyl 3-(dimethylaminomethyl)phenyl	H	но	lyind-a	n-batyl	1241
, 7	<del>  "</del>		i		
Br Br					
""	i				•
	T.				
	н	но	ικινη-α	ը/Հյոզ-ա	1736
		·			

	· .					
		н	но	r-pntyl	n-pntyl	8571
13	I Z I					
	+ (c <sub>2</sub> )	н	но	u-pnçλı	Ivînd-a	TESI .
ı	ф-(bromomethyl)phenyl	H	НО	Ivind-a	I-(żnq-u	1236
	O N(CH <sup>2</sup> CH <sup>3</sup> ) <sup>5</sup>			• •	•	,,,,,
	<u></u>	н	НО	n-pathl	a-butyl	1532

1246	n-butyl	n-butyl	OH	Н	3-(bromomethyl)phenyl
1247	n-butyl .	n-butyl	ОН	Н	ОН
1248	n-butyl	n-butyl	ОН	н	N(CH <sub>3</sub> )
1249	n-butyl	p-butyl	OH	н	CF <sub>3</sub> CO <sub>2</sub>
1250	p-butyl	n-butyl	OH	H	3-(dimethylamino)phenyl
1251	n-butyl	n-butyl	OH	Н	l-naphthyl
1252	n-butyl	n-butyl	OH	Н	1 + H(CH <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub>

1253	n-butyl	n-butyl	ОН	Н	+ N(CH <sub>3</sub> )
·		,			OCH <sub>3</sub> I
1254	n-butyl	n-butyl	OH	Н	Br +
1255	n-butyl	n-butyl	OH	н	I- I-
1256	n-butyl	n-butyl	OH	Н	3-nitrophenyl
1257	n-butyl	n-butyl	OH	H	phenyl
1258	n-butyl	n-butyl	OH	н	4-fluorophenyl
1259	ethyl	n-butyl	H	OH	Н
1260	ethyl	n-butyl	OH	H	3-hydroxyphenyl

0 S 0 N 1					
	н	но	a-butyl	n-pariyi	1/21
L Br	н	но	n-pntyl	l¢īnd- <del>a</del>	0421
1,10	н	но	n-pnţλ <u>j</u>	ηληπη-π	6971
I HÜCH2CH3)	н	но	lystud-a	Ivind-a	8921

2-piperonyl	H	но	ефуј	I/Jrnq-ti	<i>L</i> 971
OCH <sup>3</sup> + v(CH <sup>3</sup> )	н	но	lvind-n	υ-ρπίλη	1766
ф-(уполобренд)	H	НО	lytud-a	IVind-a	1792
4-fluorophenyl	Н	но	l/stud-tt	lynd-n	1764
S-piperonyl	н	но	a-pritkl	Ivino-a	1363
Z-thiophenyl	Н	но	JÆ3nq-u .	lytud-a	1562
DH E TO TO TO TO TO TO TO TO TO TO TO TO TO					
\	н	но	1/2mq-ti	i-butyl	1971

1272	n-butyl	n-butyl	· OH	Н	1- N+ + CO <sub>2</sub> H
1273	n-butyl	n-butyl	OH	н	I- (CH <sub>2</sub> ) <sub>8</sub> CH <sub>3</sub> + N—(CH <sub>2</sub> ) <sub>8</sub> CH 3 3 (CH <sub>2</sub> ) <sub>8</sub> CH 3
1274	n-butyl	n-butyl	ОН	Ħ	o CI

1275	n-butyl	в-butyl	ОН	н	F 1 + N + + N + + N + + N + + N + + N + + N + + N + + N + + N + N + + N +
1276	n-butyl	n-butyl	OH .	н	I- (CH <sub>2</sub> ) <sub>6</sub> CH(CH <sub>3</sub> ) <sub>2</sub> +  N(CH <sub>2</sub> ) <sub>6</sub> CH(CH <sub>3</sub> )   3 (CH <sub>2</sub> ) <sub>6</sub> CH(CH <sub>3</sub> ) <sub>2</sub>
1277	n-butyl	n-butyl	ОН	Н	F   CO <sub>2</sub> H

	18 + -i	н	но	į Κιπος-u	īķīnd-a	1788
3	4-рудгохуррену!	н	но	ethyl	n-pntyl	1287
	CE <sup>3</sup> CO <sup>3</sup> .	н	но	n-pniyl	lYind-n	1286
ŀ	русту	H	НО	сфуј	I/ind-n	1285
H	ф-ПиоториспуТ	H	но	lytud-n	I\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	1784
ŀ	4-рудгожупстуурспу	н	НО	l\taud-a	lytud-a	1783
ŀ	3-Плого-4-пастьохурьску	н	HO	I\tiud-a	equiyl	1282
	i l	_		16 no-t	iVind-n	1871
	V ( )	н	но	l/yud-a	l futurian	1981

	N(CH <sup>3</sup> ) <sup>2</sup>	н	но	J.Cipq-a	∫£‡nq-¤	0821
139	I- (CH <sup>5</sup> ) <sup>2</sup> CH <sup>3</sup> (CH <sup>5</sup> ) <sup>2</sup> CH <sup>3</sup>	н	но	ը. - բուչյ	ηλιη <b>η</b> -α	6/21
	I- (CH <sup>3</sup> ) <sup>4</sup> CH <sup>3</sup> (CH <sup>3</sup> ) <sup>4</sup> CH  (CH <sup>3</sup> ) <sup>4</sup> CH  (CH <sup>3</sup> ) <sup>4</sup> CH  (CH <sup>3</sup> ) <sup>4</sup> CH  (CH <sup>3</sup> ) <sup>4</sup> CH  (CH <sup>3</sup> ) <sup>4</sup> CH  (CH <sup>3</sup> ) <sup>4</sup> CH	н	но	Į£inq−o	į/sinq-a	<b>8</b> LZ I

1289	n-butyl	n-butyl	ОН	н	I- (CH <sub>2</sub> ) <sub>7</sub> CH <sub>3</sub> + N—(CH <sub>2</sub> ) <sub>7</sub> CH 3 (CH <sub>2</sub> ) <sub>7</sub> CH <sub>3</sub>
1290	n-butyl	n-butyl	OH	Н	F HO CF <sub>3</sub> CO <sub>2</sub> N +
1291	n-butyl	n-butyl	ОН	н	F CF <sub>3</sub> CO <sub>2</sub>

		•			
1292	n-butyl	n-butyl	ОН	н	+ I P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub>
1293	n-butyl	n-butyl	ОН	H	1
1294	n-butyl	n-butyl	ОН	н	I- 0 1-

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-fluotophenyl	Н	НО	a-butyl	lytud-a	1302
3-теньохурьену!	H	НО	ı/sınq-u	I\frac{1}{2}	1304
·					
(CH <sup>3</sup> ) <sup>3</sup>	н	но	16jnq-u	υ-ραιλι	1303
-fdfm-dn-c	H H	но	n-butyl	p-pntyl	1302
3-methoxyphenyl 3-hydroxyphenyl	H	но	n-pankı	Vind-a	1081
H H	НО	H	erphj	a-butyl	1300
Z.,	1.57	<del>                                     </del>			
P 2(CH <sup>3</sup> CH <sup>3</sup> ) <sup>5</sup> +  +	н	но	п-ряцуі	a-buryl	6671
A(CH)					
$\uparrow$	н	но	l/tinq-a	I-pntyl	8671

143		н	но	peres	l⁄vind-a	<i>L</i> 6 <b>Z</b> 1
H	O N(CH³CH²)	н	но	J.£inq-a	lvind-n	9671
	DE (CH3)3C	н	но	Į∕sinq-u	Kinq-u	\$621

1306	n-butyl	n-butyl	ОН	н	CF <sub>3</sub>
1307	n-butyl	n-butyl	OH	н	H
1308	ethyl	n-butyl	ОН	н	F O S O O O O O O O O O O O O O O O O O
1309	n-butyl	n-butyl	ОН	Н	4-methoxyphenyl
1310	ethyl	n-butyl	OH	Н	phenyl
1311	n-butyl	ethyl	OH	Н	phenyl
1312	n-butyl	ethyl	ОН	Н	phenyi
1313	n-butyl	ethyl	OH	н	phenyl
1314	ethyl	n-butyl	OH	Н	phenyl
1315	ethyl	n-butyl	OH	Н	phenyl
1316	n-butyl	ethyl	OH	Н	phenyl
1317	n-butyl	ethyl	ОН	н	phenyl

	1 1	n-butyl	OH	H	phenyl
1318	ethyl	n-butyl	OH	— н	3-metboxyphenyl
1319	ethyl		OH	H	phenyi
1320	ethyl	n-butyl	OH	н н	phenyl
1321	n-butyl	ethyl	OH	H	
1322	n-butyl	n-butyl	Oh	n	
1323	n-butyl	n-butyi	OH	н	N N N N N N N N N N N N N N N N N N N
1324	n-butyl	n-butyl	OH	н	1- N+ +
1325	n-butyl	p-butyl	OH	н	4-((diethylamino)methyl)phenyl
1,72,7	A-July1			<del></del>	

361	CE <sup>3</sup> CO <sup>5</sup>	н	но	r-pangaj	n-pm3,j	1661
	E CONTRACTOR OF THE PROPERTY O	н	но	Anq−u	JAmq-a	OEET

			<del></del>			
	O THE CE <sup>3</sup> CO <sup>5</sup>	н	но	pariyi	JÁINQ-U	62£1
140	+ N -1 -1	н	но	peng-u	u-pniλ	8261
-  -	Varidoboi-è-yxarbyd-b-orouft-è	Н	но	n-butyl	I/Jud-a	LZEI
	HO HO CHO CHO CHO CHO CHO CHO CHO CHO CH					
1	$\uparrow$	н	но	i-butyi	r-pntyl	1326

+ .N(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>

PCT/US00/02503

PCT/US00/02503

	-			-	
1335	n-butyl	n-butyl	ОН	Н	I- N + N
1336	n-butyl	n-butyl	ОН	н	I- 0 \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \
1337	n-butyl	n-butyl	ОН	н	I (H <sub>3</sub> C) <sub>3</sub> N +

H

n-butyl

n-butyl

1333

1334

n-butyl

n-butyl

ОН

	-N++N+					
7	_1	н	но	1/smq-ti	υ-ρπιλη	<b>#</b> \$£1
7	OF THE CF3CO2	н	но	u-pnţλ	p.kjnq-u	ESEI
	Br- OCH <sub>3</sub> CH <sub>2</sub> CH <sub>3</sub> CH <sub>3</sub> CH <sub>3</sub> D <sub>8</sub> H <sub>3</sub> O	н	но	յ <b>նյո</b> գ-ս	· [Amq-u	· ZSEI

	CF <sub>3</sub> CO <sub>2</sub> (CH <sub>3</sub> CH <sub>2</sub> )(CH <sub>3</sub> )r <sub>N</sub> (CH <sub>3</sub> ch <sub>2</sub> )r <sub>N</sub> (CH <sub>3</sub>			,	r.pnq-u	
	<u> </u>	Н	HO	ιζιπη-α Ιζιπη-α	lytud-a	1351
	3-fluoro-4-methoxyphenyl	H	но	ικιτο-α	crpyl	9451
	phenyl	н	HO	lytudozi lytud-n	isobutyl	8461
15	русилу	H	но	Içtud-a	1çind-a	7451
<u>`</u>	3-цполо-4-шепрохуррену	Н	НО	n-butyl	egylj	9461
	bpenyl	H	но	Içind-a	esph	2451
	phenyl	H	HO	[ζητις-α	n-priyl	1344
	3-Плото-4-пленюхурьену	H	HO	D-pntA1	eapyl	1343
	phenyl	Н	но	D-butyl	n-prityl	Z451.
	lynoradiq-2	H	НО		n-butyl	1961
	3-metboxyphenyl	н	acetoxy	lyind-a	P-butyl	1340
	ζ-biperonyl	н	но	сфу	Attiq-u	UPEI
	С(СНЭ)					
- 1	Ö '	H	но	Įλinq-α	lyind-a	1336
	←-metroxyphenyi	н	но	n-butyl	a-butyl	8551

1358	n-butyi	n-butyl	ОН	н	I- + P(CH <sub>2</sub> CH <sub>3</sub> )
1359	n-butyl	n-butyl	ОН	Н	
					1- N+

n-butyl

n-butyl

n-butyl

ОН

1355

1356

1357

n-butyl

n-butyl

n-butyl

S (CH <sup>2</sup> )		2HN	н	но	∣Æmq-a	Į∕snq-ū	<b>+9</b> £1
	156	N (CH²)					6961
H HO King-u King-u Zog				·			7961

155		н	но	į∕inq-a	[Kinq-a	1961
	Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z	н	но	Į£inq−a	լՀյոզ-ս	1360

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1365	n-butyl	n-butyl	OH .	H	1- 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
1366	n-butyl	n-butyl	ОН	Н	F I N + N + N + N + N + N + N + N + N + N
1367	n-butyl	n-butyl	ОН	н	I- N + N

1368	n-butyl	n-butyl	ОН	Н	
1369	n-butyl	n-butyl	ОН	н	

	Н	но	į£inq−u	i Krnd-a	SZEI
091	н	но	րչուգ-ս	ү/үнд-а	7/E1
	 н	но	į∕sinq-u	Į Kinq-a	ELEI

	-1 E	·	но	į£inq-u	Į King-u	ZLE1
154	N + N - 1 O	н	но	ı£ınq-u	<b>1</b> 6311 <b>0</b> -0	1761
١		н	но	ıkınq-u	n-pntλį	0461

1376	o-butyl	n-butyl	ОН	н	$\begin{array}{c c}  & & & \\  & & & &$
1377	n-butyl	n-butyl	ОН	Н	I- + N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub>
1378	n-butyl	n-butyl	ОН	Н .	0 + N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub>
1379	n-butyl	n-butyl	OH	Н	1 <sup>-</sup> + N(CH <sub>2</sub> CH <sub>3</sub> )

1380	n-butyl	n-butyl	ОН	Н	I-
1381	n-butyl	n-butyl	ОН	н	+ N(CH <sub>2</sub> CH <sub>3</sub> )
	·				
1382	n-butyl	n-butyl	OH	н	1- +N

ı	н	но	l⁄trud-a	a-pntyl	1388
1 (CH <sup>3</sup> CH <sup>3</sup> ) <sup>3</sup>	н	но	րերոգ-ս	a-pniyl	<b>1851</b>
O (CH <sup>3</sup> CH <sup>3</sup> )		, no	Leaved -	board =	
<b>1</b>	н	но	ը-քուֆլ	a-patyl	9851

		н	но	J.Linq-u	յ <i>է</i> սոգ-ս	\$861
163	L + + + + + + + + + + + + + + + + + + +		·			
	<u>_1</u>	н	но	p-pnt/l	n-parkl	1384
	++2					
L	· I	н	но	a-butyl	p-pntλl	1383

1389	n-butyl	n-butyl	OH	111	
				Н	
1390	n-butyi	n-butyl	·	Н	
1391	n-butyl	n-butyl	ОН	н	F O N +

1392	n-butyl	n-butyl	ОН	Н	$\downarrow$
	·				I-
1393	n-butyl	n-butyl	ОН	н	N O J
		·			1-
. 1394	n-butyl	n-butyl	ОН	н	N + N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub>

	N(CH <sup>3</sup> ) <sup>3</sup>					
$\vdash$		H	но	1\text{V1nd-a}	n-predj	1400
891	-N++N					
-		н	но.	I-butyl	lytud-a	1366
	+ N					
1	-I /	н	но	n-butyl	n-prask	1398

_						
	+ + T	н	но	г-рагуј	king-a	<i>L</i> 681
	n(ch <sup>5</sup> cH <sup>3</sup> ) <sup>3</sup>					2001
167	-1					
L	/   \	н	но	n-butyl	ը/ազ-ա	9681
	-1 o				. ,	
	<b>+</b>	н	но	ηζιης-α	ը/փոզ-ս	1395

1401	n-butyl	n-butyl	OH	Н	<u>l</u>
]				Ì	
	ĺ				
i					
					1 12
j	ļ				`\$—ОН
		Ì			
1402	n-butyl	n-butyl	ОН	н	ī
				·	
l I					
•					
1403	n-butyl	n-butyl	ОН	н	, , , , , , , , , , , , , , , , , , , ,
					1-
				1	
]					
			<u> </u>		

1404	n-butyl	n-butyl	OH	. Н	4
					1-
1405	n-butyl	n-butyl	ОН	H	I-
					CO₂H
1406	n-butyl	n-butyl	ОН	Н .	<del>V</del> <del>V</del>
					1-
					+
					N N

+ 1					·
1- E	н	но	l⁄ind-n	u-pntλ1	7171
H <sub>6</sub> Od N O	н .	но	п-рику	ракуу	1141
H <sup>2</sup> CO <sup>2</sup> H		НО	n-prit\j	n-butyl	1410

_	· ·					
	N(CH <sup>2</sup> CH <sup>9</sup> )					
L	_1	н	но	I-butyl	I-thud-a	60 <b>†</b> I
121	T I I I I I I I I I I I I I I I I I I I			·		
H		н	HO.	n-butyl	α-ραίλ]	1408
	-1					
		н	но	ը-թունլ	n-butyl	L041

					H + h
1414	n-butyi	n-butyl	ОН	н	1- N

1415	n-butyl	n-butyl .	OH .	н	I-
1416	n-butyl	n-butyl	OH	Н	I-  N H N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub>
1417	n-butyl	n-butyl	ОН	H	I- N

88
0/475
õ
=

	C(CH <sup>5</sup> VI(CH <sup>5</sup> CH <sup>3</sup> ) <sup>3)3</sup> O I I			:		
175	- I - I					
	<del>_</del>	н	но	Iv)nd-a	ո-բունվ	1419
.	ОН	:				
	+ OH OH	·				
	_1	н	но	թերոգ-ս	ικπο-α	1418

921	N+	н	но	[Asnq-u	į/smq-u	1421
	H H	н	но	ivad-a	Ivind-n	1450

1422	n-butyl	n-butyl	OH	<b>H</b>	1 + N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub>
1423	n-butyl	n-butyl	ОН	н	1 + N
1424	n-butyl	n-butyl	ОН	н	I +

1425	n-butyl	n-butyl	ОН	Н	I-
					+ N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub>
1426	n-butyl	n-butyl	OH	Н	\ \ \ \
					I-
					+ N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub>
1427	n-butyl	n-butyl	ОН	Н	H
		•			1- \
					N+ OH
			L	<u> </u>	

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	J. O. J. O.	н	но	a-pniyl	JAinq-u	1435
180	O + (CH <sup>3</sup> CH <sup>3</sup> ) <sup>3</sup>	н	но	u-pntyl	<b>γέλη</b> ας-τε	l E p I
	+ 1	•			P3-74	teri
	Br	н	но_	ntinq-u	lVind-n	1430

129	Br Br					
	HO S	н	но	JAmq-u	-panyt	6241
		l н	но	f/tinq-a	l/stro-a	8201

1433	n-butyi	n-buryl	ОН	н	F
1434	n-butyl	n-butyl	ОН	Н	1 + N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub>

	135	n-butyl	n-butyl	ОН	Н	F OH OH
	36	n-butyl	n-butyl	ОН	н	
14	37	n-butyi	n-butyl	ОН	Н	Br - + P(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub>

3, 0, (	н	но	n-butyl	l/smd-a	1444
	н	но	յՀյոգ-ս	ι,έ,ιης−α	1443
CO <sub>2</sub> H  CO <sub>3</sub> H	н	но	լչնոգ-ս	ե-թուչոյ	Z <b>++1</b>

_						
	P (CH <sub>2</sub> CH <sub>3</sub> )3	н	но	Iyind-a	n-pntλj	1991
183		н	но	p-prikl	a-pniyî	1440
	8 N(CH <sup>3</sup> CH <sup>3</sup> ) <sup>3</sup> + 1					
	y(CH <sup>2</sup> CH <sup>3</sup> ) <sup>3</sup> + 1	н	но	JÁmq-u	p-pniÀi	1436
	\	н	но	a-butyl	JAmq-u	1438

	. [				
1446	n-butyl	n-butyl	ОН	н	Br SO <sub>3</sub> Na
1447	n-butyl	n-butyl	ОН	н	Na <sup>+</sup>
1448	n-butyl	n-butyl	ОН	н	so <sub>3</sub> -

1449	n-butyl	n-butyl	ОН	н	1- ++
1450 1451	n-butyl n-butyl	n-butyl n-butyl	ОН	H H	phenyl SO <sub>3</sub> H

	onims-7	Н	671
	7-(O-benzylcarbamato)	Н	871
	onima-7	н	LZI
	(oremedianlysnad-O)-7	н	176
	at the 8-position +		961
	Ommsiyad-7	н	155
	onime-7	н	133
<del></del>	onims-7	R	175
	7-(O-benzylcarbamato)	Н	171
<u>.                                 </u>		H	170
	7-(O-tert-butylearbarnato)	H	611
	7-(O-benzylearhanato)	н	118
	7-(O-benzylearbanato)	н	<u> </u>
	7-(O-benzylcarbamato)	н	911
	(O)-Carbamato)	н	511

onima-7	н	<b>711</b>
Ontare-V	н —	
onims-/	H	113
outine-/	H	115
7-acetamido		111
onims-7	н	011
7-(hexylamido)	Н	109
	н	801
onime-7	н	<i>L</i> 01
7-(2'-bromoscetamido)	H	901
7-methanesulfonamido	н	S01
7-dimethytamino	Н	104
əbiboi muinommslyhəmin-7	H	103
notiteoq-Y arti 1s abiboi muinommalydtamrit-Y	H	Z01
HO, M. S. S. S. S. S. S. S. S. S. S. S. S. S.		
0	н	101
p( <sup>7,5)</sup>	· 180	Compound Number

131	н	at the 7-position
132	Н	N N N N N N N N N N N N N N N N N N N

134 135 ОН

190

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at the 7-position		
OH		
J. + 1° C		
0,0	н	6£1
noinizoq-18  Vxetissis 8	H	8£1
OH		
7°+0+0+0+0+0+0+0+0+0+0+0+0+0+0+0+0+0+0+0		
	н	<b>4</b> £1
L		

onine-7	НН	786
onims-\(\(\triangle \)	H	788
onima-7	Н	L87
(O-benzykanato)	H	987
(onilodqrom-'4)-7	н	784
Г-тефуј	4-fluoro-phenyl	283
у-шефуј	Н	787
очеруние стануру	н	187
· vxorbam-7	н	. 082
	н	579
Улефоху	н	872
7-тестоху	H	LLZ
oroufi-7	H	927
oroufi-7	3-тенроху-распу!	SLZ
orouli-7	H	\$LZ
ozoufi-7	4-tlucto-phenyl	273
отол-Г	3-тесроху-ррепу]	7.LT
· omord-?	н	1/2
7-руфоху	Н	270
7-тефоху	4-tluoro-phenyl	697
γxotham-Γ	н	897
7-тефоху	Н	767
7-һуфгоху	Н	997
	phenyl	
7-тефоху	3-trifluoro-methyl-	392
7-шефоху	Н	764
7-тефоху	3-тейоху-распуі	593
у-тефоху	H	797
(lynibi)-7.	H	144
7-тепуйтегеврю	Н	143
	1	
у-шеңуулыссары	3-methoxy-phenyl	741

290	H	7-amino
291	H	7-(O-benzylcarbamato)
292	H	7-amino
293	Н	7-benzylarnino
294	Н	7-dimethylamino
295	Н	7-amino
296	Н	7-amino
1000	Н	7-dimethylamino
1001	н	7-dimethylamino
1002	- Н	7-dimethylamino
1003	H	7-dimethylamino
1004	Н	7-dimethylamino
1005	Н	7-dimethylamino
1006	Н	7-dimethylamino
1007	H	7-dimethylamino
1008	H	7-dimethylamino
1009	H	7-dimethylamino
1010	H	7-dimethylamino
1011	H	7-dimethylamino
1012	н	7-dimethylamino; 9-methoxy
1013	Н	7-dimethylamino
1014	Н	7-dimethylamino; 9-methoxy
1015	Н	7-dimethylamino
1016	Н	7-dimethylamino
1017	Н	7-dimethylamino
1018	H	7-dimethylamino
1019	Н	7-dimethylamino
1020	Н	7-dimethylamino
1021	н	7-dimethylamino
1022	н	7-dimethylamino
1023	Н	7-dimethylamino
1024	H	7-dimethylamino
1025	H	7-dimethylamino

1026	H	7-dimethylamino
1027	H	7-dimethylamino
1028	H	7-dimethylamino
1029	Н	7-dimethylamino
1030	H	7-dimethylamino
1031	Н	7-dimethylamino
1032	Н	7-dimethylamino
1033	н	7-dimethylamino
1034	Н	7-dimethylamino
1035	H	7-dimethylamino
1036	H	7-dimethylamino
1037	н	7-dimethylamino
1038	Н	7-dimethylamino
1039	н н	7-dimethylamino
1040	H .	7-dimethylamino
1041	Н	7-dimethylamino
1042	Н	7-dimethylamino
1043	н	7-dimethylamino
1044	Н	7-dimethylamino
1045	н	7-dimethylamino
1046	Н	7-dimethylamino
1047	Н	7-dimethylamino
1048	Н	7-dimethylamino
1049	Н	7-dimethylamino
1050	Н	7-dimethylamino
1051	H	7-dimethylamino
1052	H	7-dimethylamino
1053	H	7-dimethylamino
1054	н	7-dimethylamino
1055	Н	7-dimethylamino
1056	H	7-dimethylamino
1057	Н	7-dimethylamino
1058	Н	7-dimethylamino

195

7-dimethylamino 7-dimethylamino 7-dimethylamino 0601 6801 H H H H H H H H H odimethylamino

- contractorianino

- contract \$801 \$801 \$801 \$801 2801 1801 6401 4401 4401 9401 9401 9401 H H H <u>Н</u> Н Н Н \$701 1701 0/01 6901 8901 4901 9901 9901 9901 <u>н</u> н H H H H H H E901 Z901 1901 0901

ommsiydtərmb-7	Н	1153
orims/yth>mib-7	H	1172
onimslyth3mib-f	н	1711
onimalythamib-7	Н	1120
7-dimethylamino	H.	6111
ominstythemib-7	Н	1118
onimslythsmib-7	Н	4111
7-dimethylamino	н	1116
7-dimethylamino	н	SILL
ommslythom-7	Н	PIII
7-dimethylamino	Н	EIII
omimstythamin-7	н	1115
ominachydamino-7	н	1111
7-dimethylamino	н	1110
orimathylamino-7	Н	6011
7-dimethylamino	Н	8011
onimslythamin-7	Н	L011
onimeltythamin-T	н	9011
oninelythemib-7	Н	5011
7-фімефувацію	H	1104
7-dimethylamino	Н	1103
7-dimethylamino	H	7011
7-dimethylamino	Н	1011
7-сішець/рашіно	Н	0011
	н	6601
7-dimethylamino	н	8601
orimaty/domith-T	H	<u> </u>
ommslythsmib-7	н	9601
ominalydbsmib-7	н	\$601
-7-dimethylamino	н	<del>\$601</del>
7-dimethylamino	Н	£601
orimethylamino-7	Н	Z601
· onimethylamino	н	1601

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1124	H	7-dimethylamino
1125	H	7-dimethylamino
1126	н	7-dimethylamino
1127	H	7-dimethylamino
1128	Н	7-dimethylamino
1129	Н	9-dimethylamino
1130	H	7-dimethylamino
1131	Н	7-dimethylamino
1132	Н	7-dimethylamino
1133	Н	7-dimethylamino
1134	н	7-dimethylamino
1135	Н	7-dimethylamino
1136	Н	7-dimethylamino
1137	H	9-(2',2'-dimethylhydrazino)
1138	Н	7-dimethylamino
1139	н	7-dimethylamino
1140	н	7-(2',2'-dimethylhydrazino)
1141	н	7-ethylmethylamino
1142	Н	7-dimethylamino
1143	3-fluoro-4-	7-dimethylamino
	methoxy-phenyl	
1144	H	7-dimethylamino
1145	H	9-dimethylamino
1146	Н	7-dimethylamino
1147	H	7-diethylamino
1148	Н	7-dimethylsulfonium, fluoride salt
1149	Н	7-ethylamino
1150	H	7-ethylmethylamino
1151	H	7-dimethylamino
1152	H	7-(ethoxymethyl) methylamino
1153	H	7-methylamino
1154	Н	9-methoxy
1155	H	7-methyl

1156	H	7-methylmercapto
1157	Н	7-fluoro;
		9-dimethylamino
1158	H	7-methoxy
1159	H	7-dimethylamino
1160	H	7-diethylamino
1161	Н	7-dimethylamino
1162	Н	7-dimethylamino
1163	Н	7-methoxy
1164	н	7-methoxy
1165	Н	7-trimethylammonium iodide
1166	Н	7-trimethylammonium jodide
1167	н	7-dimethylamino
1168	н	7-trimethylammonium jodide
1169	н	8-dimethylamino
1170	Н	7-ethylpropylamino
1171	Н	7-dimethylamino
1172	Н	7-methoxy
1173	Н	7-ethylpropylamino
1174	н	7-phenyl
1175	Н	7-methylsulfonyl
1176	Н	9-fluoro
1177	H	7-butylmethylamino
1178	H	7-dimethylamino
1179	н	8-methoxy
1180	Н	7-trimethylammonium iodide
1181	Н	7-butylmethylamino
1182	Н	7-methoxy
1183	н	7-fluoro
1184	н	7-fluoro; 9-fluoro
1185	H	7-fluoro
1186	н	7-fluoro; 9-fluoro
1187	н	7-methyl

ominstydtsmib-7	Н	1549
onimaly dramits-7	н	1748
onimskythomib-7	Н	L\$Z1
onimetlythemin- 7	н	1746
ommslythamib-7	Н	1542
7-(1)-freehythythzeri-(1)-(	Н	1244
onimalyth∋mib-7	Н	1543
onimalythamib-7	Н	1747
7-dimethylamino	Н	1521
ominuslythэmib-7	Н	1240
onimslythemib-7	н	1239
7-dimetylylamino	н	1238
onimslyth>mib-7	н	LEZI
orimaly/hamib-7	Н	1736
7-dimethylamino	H	1535
onimstyhtemib-7	н	1234
onimalyddamib-7	H	1233
onimalyddamin-9	н	1232
onimalythamib-7	н	1531
orouf1-7		7,00.
9-dimethylamino;	_ _ н [	1230
onimalythomin-7	Н	1339
O-dimetlythemin-C		
	H	1228
ommslylud-rest)-7	Н	LZZI
omond-7	Н	1226
otimely/lemin-7	H	1325
отоиЛ-7	н	1224
уш-тустрон 1	1	7.00
tomord-8	н	1333
7-cthylamino	H	1333
onimalythemib-7	H	1221
onimslyqorqozi-7	H	1220

7-dimethylamino	н	1516
9-methylsulfonyl	H	1218
-dimethylamino	н	
7-bromo	H	1217
9-акфульнсара		9171
(obimennollynbann-M)-7	Н Н	1512
CI:		1514
7-dimethylamino	methoxy-phenyl	
(onilodquon-1-)-9	-P-orouli-E	1213
7-dimethylamino	Н	1212
orimethylamino 7-dimethylamino	Н	1211
	н	1510
7-dimethylphenyl	н	6071
onimaly(themib-7	н	1208
onimsly(themip-f	н	L0Z1
onimstythemib-7	н	1506
onimatyMamino-7	H	1702
7-тейоху	н	1504
(lymandylynd-nas-/)-7	н	1503
γχούσειτ-Γ	н	1505
7-methyl	н	1021
onimslythamib-C	bycuλi	1200
onimsly@bmib-V	н	6611
үхогрэт-Г	Ĥ	8611
(obirmsmrollydiəm-V/)-7	H	4611
7-тестьоху	H	9611
7-(4'-methylpiperazin-1-yl)	ਜੰ ਜ	
7-dimethylamino	н	5611
onimely/hamib-7	H	<del>\$611</del>
		1193
Ахолуйч-Д	Н Н	7611
omord-7	Н	1611
sbiboi muinommslydtəmin-V	Н	0611
7-trimethylamming indiae	Н	6811
-bibei miinommskuttamitt-f	н	1188

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1250	
1252	
1253   H   7-dimethylamino   1254   H   7-dimethylamino   1255   H   7-dimethylamino   1255   H   7-dimethylamino   1256   H   7-dimethylamino   1256   H   7-dimethylamino   1257   1258   1	
1254         H         7-dimethylamino           1255         H         7-dimethylamino           1256         H         7-dimethylamino	
1255 H 7-dimethylamino 1256 H 7-dimethylamino 7-dimethylamino	
1256 H 7-dimethylamino	
- Cancer Junior	
1257 H 8-bromo: 7-dimethylamine	<del></del>
1258 H 9-(tert-butylamino)	
1259 phenyl 7-dimethylamino	
1260 H 7-dimethylamino	
1261 H 7-dimethylamino	
1262 H 7-dimethylamino	
1263 H 7-bromo	
1264 H 7-isopropylamino	
1265 H 9-isopropylamino	
1266 H 7-dimethylamino	
1267 H 7-carboxy, methyl ester	
1268 H 7-dimethylamino	
1269 H 7-dimethylamino	
1270 H 7-dimethylamino	
1271 H 7-dimethylamino	
1272 H 7-dimethylamino	
1273 H 7-dimethylamino	
1274 H - 7-dimethylamino	
1275 H 7-dimethylamino	
1276 H 7-dimethylamino	
1277 H 7-dimethylarnino	
1278 H 7-dimethylamino	
1279 H 7-dimethylamino	
1280 H 7-dimethylamino	
1281 H 7-dimethylamino	
1282 H 7-trimethylammonium iodide	

1283	H	7-dimethylamino
1284	H	9-ethylamino
1285	H	7-dimethylamino
1286	Н	7-dimethylamino
1287	H	7-dimethylamino
1288	н	7-dimethylamino
1289	H	7-dimethylamino
1290	н	7-dimethylamino
1291	Н	7-dimethylamino
1292	н	7-dimethylamnio
1293	H	7-dimethylamino
1294	н	7-dimethylamino
1295	H	7-dimethylamino
1296	Н	7-dimethylamino
1297	Н	7-dimethylamino
1298	н	7-dimethylamino
1299	н	7-dimethylamino
1300	phenyl	7-dimethylamino
1301	Н	7-trimethylammonium iodide
1302	Н	9-hydroxy
1303	Н	7-dimethylamino
1304	н	7-tert-butylamino
1305	Н	9-methylamino
1306	н	7-dimethylamino
1307	4-methoxy-phenyl	9-(4'-morpholino)
1308	Н	7-dimethylamino
1309	Н	9-fluoro
1310	н	7-amino
1311	н	7-(hydroxylamino)
1312	н	8-hexyloxy
1313	H	8-ethoxy
1314	H	7-(hydroxylamino)
1315	H	7-(nydroxylammo) 7-(hexyloxy)

onimslythemib-7	н	1362
7-dimethylamino	н	1981
onimslythamib-7	н	09E1
onimslydtsmib-7	Н	65£1
onimalydismib-7	н	1328
onimslythamib-7	н	LSEI
onimslyAbamib-7	н	1326
7-dimely/lamino	н	SSEI
orimsly/fibruib-7	н	1354
7-dimethylamino	н	ESE1
onimelythamin-7	н	1352
onimethyltəmino	. н	1551
7-trimethylammornium iodide	н	OSEI
7-dimethylamino	н	67E1
7-dimethylamino	н	1348
onimslythamin-7	н	1347
	1	1 4751
at the 8-position	, A	Zni
O O O O O O O O O O O O O O O O O O O	н	9481
obshoi muinommalydromira-7	<u>н</u> н	94E1
onimalydramia-T  obiboi muinommalydramia-T  oog  oog  oog  oog  oog  oog  oog  o	<u>н</u> н н	97E1 97E1
onime-T onimethylienin-T onimethylienin-T ooliele oolie oo	Н Н Н	97E1 57E1 77E1
(lynadquoult-1s)-7  onima-7  -7-dimedylamino-7  onimalylamino-7  onimalylamino-7  onimalylamino-7  onimalylamino-7  onimalylamino-7	H H H H	99E1 59E1 99E1 59E1 29E1
onimalythamib-\(\triangle \)  (I)(mpdqnonin-\(\triangle \)-\(\triangle \)-\(\triangle \)  onima-\(\triangle \)-\(\triangle \)  onimalythamib-\(\triangle \)  ohiboi muinonmalythamin-\(\triangle \)  ooliconal (mpanin-\(\triangle \))	H H H H H	9751 5751 7751 7751
iythan-7 onimal-7 onimalyhamib-7 (ivandonouh-1»-7 onima-7 onima-7 onimalyhamin-7 obiloo iminominalyhamin-7 obiloo iminominalyhamin-7	H H H H H H	99E1 59E1 99E1 29E1 29E1
orinnslythemib-T    Vermenty	H H H H H H H	90E1 50E1 50E1 50E1 70E1
(/kinserach/dytharan-/h)-/ onimal/dhymib-/ / kinam-/ onimal/dhymib-/ (/kinadyonulh-/h)-/ onima-/ onimal/dhymib-/ onimal/dhymid-/ onimal/dhymid-/	H H H H H H H	97E1 57E1 57E1 57E1 17E1 07E1
onimalydaemia-f  (lydisensidylydaem-b-f  onimalydaemia-f  lydisen-f  onimalydaemia-f	H H H H H H H H	97E1 57E1 57E1 57E1 77E1 07E1 6EE1
odimedy/anmib-7  odimedy/anmib-7  odimedy/perdexinyl)  forestylpiperazinyl)  odimedy/anmib-7  odimedy/anmib-7  odimedy/anmib-7  - (-(incethyleni)  - (-(incethyleni)  odied-7  odimedy/anmib-7  odied-7  odimedy/anmib-7  odied-9  o	H H H H H H H H H	99E1 59E1 99E1 59E1 29E1 19E1 09E1 66E1 86E1
oninselyhamib-7  oninselyhamib-7  oninselyhamib-7  -7-dimedylamino-7  oninselyhamib-7  oninselyhamib-7  -1-dimedylamino-7  oninselyhamib-7  oninselyhamib-7  -1-dimedylamino-7  oninselyhamino-7  oninselyhamino-1	H H H H H H H H H H H H H H H H H H H	9761 5761 5761 5761 1761 1761 6601 8001 8001 4001
orimetly/lamino  7-dimethylamino  7-dimethyliperazinyl)  7-dimethylamino  7-dimethylamino  7-dimethylamino  7-dimethylamino  7-dimethylamino  7-dimethylamino  7-dimethylamino  7-dimethylamino  7-dimethylamino  9-dimethylamino  1-dimethylamino  1-dimethylamino  9-dimethylamino  1-dimethylamino	H H H H H H H H H	97E1 57E1 57E1 57E1 57E1 100E1 6EE1 8EE1 4EE1 9EE1

	7-dimetly lamino	Н	7551
	7-dimethylamino	н	1661
	onimely/lamino-f	н	1330
	onimelythemib-7	н	1339
1	onimslythemib-7	Н	1328
	onimelythemib-7	Н	LZE1
	onimslythemib-7	Н	1326
	onimelythemib-7	Н	1325
	onimslythamib-7	н	1324
	ommslythemib-7	н	1323
	7-dunethylamino	Н	1322
203	O S S S S S S S S S S S S S S S S S S S	н	1261
	orims-C	H	1320
	orouft-7	н	6161
	ommelythemib-7	н	8151
	motrized-8 art 1s		
	→ (CH³)³ +		
	_I	<u>н</u> н	LIEI
	8-руфоху	н	9151

1363	н	7-dimethylamino
1364	н	7-dimethylamino
1365	н	7-dimethylamino
1366	н	- 7-dimethylamino
1367	н	7-dimethylamino
1368	H ·	7-dimethylamino
1369	н	7-dimethylamino
1370	н	7-dimethylamino
1371	Н	7-dimethylamino
1372	н	7-dimethylamino
1373	н	7-dimethylamino
1374	н	7-dimethylamino
1375	н	7-dimethylamino
1376	. н	7-dimethylamino
1377	н	7-dimethylamino
1378	н	7-dimethylamino
1379	н	7-dimethylamino
1380	н	7-dimethylamino
1381	н	7-dimethylamino
1382	н	7-dimethylamino
1383	н	7-dimethylamino
1384	н	7-dimethylamino
1385	н	7-dimethylamino
1386	н	7-dimethylamino
1387	н	7-dimethylamino
1388	н	7-dimethylamino
1389	н	7-dimethylamino
1390	Н	7-dimethylamino
1391	н	7-dimethylamino
1392	н	7-dimethylamino
1393	н	7-dimethylamino
1394	н	7-dimethylamino
1395	н	7-dimethylamino

1396	Н	7-dimethylamino
1397	Н	7-dimethylamino
1398	Н	7-dimethylamino
1399	н	7-dimethylamino
1400	н	7-dimethylamino
1401	н	7-dimethylamino
1402	Н	7-dimethylamino
1403	Н	7-dimethylamino
1404	Н	7-dimethylamino
1405	Н	7-dimethylamino
1406	Н	7-dimethylamino
1407	н	7-dimethylamino
1408	н .	7-dimethylamino
1409	Н	7-dimethylamino
1410	Н	7-dimethylamino
1411	Н	7-dimethylamino
1412	Н	7-dimethylamino
1413	н	7-dimethylamino
1414	Н	7-dimethylamino
1415	Н	7-dimethylamino
1416	Н	7-dimethylamino
1417	H	7-dimethylamino
1418	Н	7-dimethylamino
1419	н	7-dimethylamino
1420	н	7-dimethylamino
1421	Н	7-dimethylamino
1422	Н	7-dimethylamino
1423	н	7-dimethylamino
1424	Н	7-dimethylamino
1425	Н	7-dimethylamino
1426	н	7-dimethylamino
1427	н	7-dimethylamino
1428	Н	7-dimethylamino

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selected from among the radicals disclosed in Table 2 below. Preferably, Re is Another class of compounds of particular interest comprises those 1,2benzothiazepines wherein the R1, R2, R3, R4, R6, RN and R\* radicals are hydrogen; and/or R1 and R2 are alkyl. More preferably, R1 and R2 are the hydrogen and R<sup>3</sup> is other than hydrogen; and/or R<sup>3</sup> is hydroxy and R<sup>4</sup> is same.

S

Table 2

· · · · · · · · · · · · · · · · · · ·	
8-SO2CH3 8-SCH2CH3 8-NHOH 8-NHCH3 8-NHCH3 8-NHCH3 8-NHCH3 8-NHCH3)3. I' 8-NHC(0)CH3 8-N(CH2CH3)3. I' 8-NHC(0)CH3 8-N(CH2CH3)2 8-N(CH2CH3)2 8-N(CH2CH3)2 8-N(CH2CH3)2 8-N(CH2CH3)2 8-N(CH2CH3)2 8-NHC(0)CH3 8-(N)-N-methyl- pyrrolldinlum, I' 8-(N)- methyl-pyrrolldinum, I' 8-(N)- methyl-pyrrolldinum, I' 8-(N)- M-methyl- pyrrolldinlum,	8-O(iso-propyl) 8-SCH <sub>3</sub> 8-SOCH <sub>3</sub>

ethyl n-propyl n-bunyl n-bunyl n-bunyl n-benyl chi3)3-N <sup>+</sup> - CH2CH2; n-ben n-chi3)3-N <sup>+</sup> - CH2CH2; n-ben n-chi3)3-N <sup>+</sup> - CH2- (OCH2CH2)2-O- n- n-b n-chi2O-penzine)-(N') CH2- (OCH2CH2)2-O- ph n-chi3O-p-p-ph n-chi3O-p-ph n-chi3O-p-p-ph n-chi3O-p-ph n-chi3O-p-p-ph n-chi3O-p-p-ph n-chi3O-p-p-ph n-chi3O-p-p-ph n-chi3O-p-ph n-chi3O-p-p-ph n-chi3O-p-ph n-chi3O-p-ph n-chi3O-p-ph n-chi3O-p-ph n-chi3O-p-ph n-chi3O-p-ph n-chi3D-n-chiam, 1-7,(N)-pyrrolidine n-pipenzine),(N') n-benylopienzinium, 1-7,(N)-pyrolidine n-pipenzine),(N') n-benylopienzinium, 1-7,(N)-pyrolidine n-pipenzine),(N') n-benylopienzinium, 1-7,(N)-pyrolidine n-pipenzinium, 1-7,(N)-pyrolidine n-pip	d HO- ropyl H- ayl H- propyl propyl propyl poline) CH <sub>1</sub> CH <sub>1</sub> CH <sub>2</sub> CH <sub>3</sub>	H Ph. PF-Ph. PF-Ph. PF-Ph. P-F-Ph. P-CH3)0-Ph. P-CH3)2-N-Pb. P-CH3)2-N-Pb. P-CH3)3-N-Pb. P-CH3)3-N-Pb. P-PCH3)3-N-Pb. P-PCH3)4-dimethyl-piperazine)-(N')-CH2-Pb. Ph. P-PCH3O-Pb. Ph. P-PCH3O-Pb. Ph. P-PCH3O-Pb. A, dioxymethyl-ne-Ph. P-PCH3O-Pb. A-pyridine N-methyl-4-pyridinium P-pyridine N-methyl-3-pyridinium P-pyridine N-methyl-3-pyridinium P-pyridine N-methyl-3-pyridinium P-pyridine N-methyl-3-pyridinium P-pyridine	7-methyl 7-ethyl 7-ethyl 7-ethyl 7-ethyl 7-iso-propyl 7-iso-propyl 7-iso-propyl) 7-O(iso-propyl) 7-SCH3 7-O(iso-propyl) 7-SCH2H3 7-O(iso-propyl) 7-SCH2CH3 7-NHCH3 7-NHCH3 7-NHCH3 7-NHCH3 7-NHCOOH3 7-NHCOOCH4 7-NHCOOCH4 7-NHCOOCH4 7-NHCOOCH3 7-NHCOOCH4 7-NH-idelinium, 1 ' 7-(N)-azeridine 7-(N)-v-methyl-prolidinium, 1 ' 7-(N)-N-methyl-prolidinium, 1 ' 7-(N)-N-methyl-piperazinium, 1 ' 7-(N)-N-CO)CH3-B1 ' 7-NH-CO)CH3-B1 ' 7
Ph.   Ph.   Ph.     Ph.	ropyi H.  anyi myi propyi propyi pC2HS 2O-(4- coline) CH-CH,	Ph. p-F.Ph. p-CH3)O-Ph. p-HO-Ph. m-CH3)O-Ph. p-HO-Ph. m-HO-Ph. m-HO-Ph. m-HO-Ph. m-HO-Ph. m-HA-Ph. p-HO-Ph. m-HA-Ph. p-HO-Ph. m-HA-Ph. p-HO-Ph. m-HA-Ph. p-HA-Ph. m-HA-Ph. T. p-(CH3)3-N*-Ph. T. p-(CH3)3-N*- CH2CH2)2-O- Ph. T. m-(CH3)3-N*- CH2CH2)2-O- Ph. T. m-(CH3)3-N*- CH2CH2)2-O- Ph. T. p-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph. T. p-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph. T. p-CH3O-Ph. 3.4,dioxymethylene-Ph. m-T, p-CH3O-Ph. 3.4,dioxymethylene-Ph. m-F, p-CH3O-Ph. 3.4,dioxymethylene-Ph. m-F, p-CH3O-Ph. 3.4,dioxymethylene-Ph. m-F, p-CH3O-Ph. 3.4,dioxymethyl-pyridinium. T- pyridine N-methyl-4-pyridinium. T- pyridine N-methyl-3-pyridinium. T- pyridine	7-chtyl 7-iso-propyl 7-iso-propyl 7-iso-propyl 7-OH 7-OH 7-OH 7-OH 7-OH 7-OH 7-OH 7-OH
aryi  p-F-Ph  mmy)  m-F-Ph  buryi  p-G130-Ph  buryi  p-HO-Ph  buryi  p-HO-Ph  p-HO-Ph  p-G130-Ph  p-G130-Ph  p-G130-Ph  p-G130-Ph  p-G130-Ph  p-G130-Ph  p-G130-Ph  p-G130-N-Ph  I. p-G130-N-Ph  I. p-G130-N-Ph  I. p-G130-N-Ph  I. p-G130-N-Ph  I. p-G130-N-Ph  I. p-G130-N-Ph  I. p-G130-N-Ph  I. p-G1212-0-Ph  I. p-(N.N-dimethyl-  piperazine)-(N')  CH2-  CH2-CH2)2-O-Ph  I. m-(N.N-dimethyl-  piperazine)-(N')  CH2-  (OCH2CH2)2-O-Ph  I. m-GN-dimethyl-  piperazine)-(N')  CH2-  GOH2CH2)2-O-Ph  I. m-CH30-Ph  J-gyridine  N-methyl-4-pyridinium,  I.  J-pyridine  N-methyl-2-yi  S-Cl-thiemyl-2-yi  S-Cl-thiemyl-2-yi  S-Cl-thiemyl-2-yi  S-Cl-thiemyl-2-yi	ayi ayi mmy) mmy) sayi sayi sayi sayi sayi sayi sayi sayi	P-F-Ph. m-F-Ph. p-CH30-Ph. p-CH30-Ph. p-HO-Ph. p-HO-Ph. m-HO-Ph. M-M-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- ph. l', m-(N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- ph. l', m-CH3O-Ph. 3.4,dioxymethylene-Ph. m-H, p-CH3O-Ph. 3.4,dioxymethylene-Ph. m-H, p-CH3O-Ph. 3.4,dioxymethylene-Ph. 3.4,dioxymethyl-a-pyridinium. l- p-pyridine N-methyl-4-pyridinium. l- p-pyridine N-methyl-3-pyridinium. l- p-pyridine	7-iso-propy! 7-iso-propy! 7-cer-buty! 7-OH 7-OCH 7-OCH 7-OCH 7-OCH 7-OCH 7-SCH2GH 7-SCH2GH 7-SCH2GH 7-SCH2GH 7-SCH2GH 7-SCH2GH 7-NHCH 7-NHCH 7-NHCH 7-NHCH 7-NHCH2CH 7-NHCH2CH 7-NHCH2CH 7-NHCH2CH 7-NHCH2CH 7-NHCH2CH 7-NH-COC 7-NN-A-methyl- problidmium, I' 7-(N)-N-methyl- morpholimium, I' 7-(N)-N-methyl- morpholimium, I' 7-(N)-N'
my) p-CH <sub>3</sub> O-Ph- bunyl p-CH <sub>3</sub> O-Ph- pennyl p-CH <sub>3</sub> O-Ph- pennyl p-CH <sub>3</sub> O-Ph- pennyl p-CH <sub>3</sub> O-Ph- polyl-Ph- polyl-Ph- polyl-Ph- polyl-Ph- polyl-Ph- polyl-Ph- p-H <sub>2</sub> N-Ph- r, p-(CH <sub>3</sub> ) <sub>3</sub> N-Ph- r, p-(N,N-dimethyl- piperazine)-(N')- CH <sub>2</sub> . (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- ph- piperazine)-(N')- CH <sub>2</sub> . (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- ph- piperazine)-(N')- CH <sub>2</sub> . (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- ph- piperazine)-(N')- CH <sub>2</sub> . (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- piperazine)-(N')- CH <sub>2</sub> . (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- piperazine)-(N')- CH <sub>2</sub> . (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- piperazine)-(N')- CH <sub>2</sub> . (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazine)-(N')- CH <sub>2</sub> .  piperazin	my) propyl propyl pcanyl pcoline) CH <sub>1</sub> CH <sub>3</sub>	m.F.Ph. p-CH3,0.Ph. p-H0-Ph. m.CH3,0.Ph. m.CH3,0.Ph. m.(CH3,0.Ph. m.(CH3,3).N-Ph. r. m(CH3)3.N-Ph. r. m(CH3,0-Ph. r. m(N.N-dimethyl- piperazine)-(N')- CH2. (OCH2CH2)2-O- Ph. (OCH2CH2)2-O- Ph. (OCH2CH2)2-O- Ph. m-CH3,0-Ph- 3.4,dioxymethylene-Ph. m-CH3,0-, p-F.Ph. 4-pyridine N-methyl-4-pyridinium r. p-pyridine N-methyl-4-pyridinium r. p-pyridine N-methyl-3-pyridinium r. p-pyridine	7-tert-bunyl 7-OCH 1-OCH 1-OCH 1-OCH 1-OCH 1-OCH 1-SCH
P.CH30-Ph- propyl p-HO-Ph- p-H	Exyl propyl propyl pentyl	p-CH3O-Ph- p-HO-Ph- m-CH3O-Ph- m-CH3O-Ph- m-CH3)2-N-Ph- m-(CH3)3-N <sup>+</sup> -Ph- r, p-(CH3)3-N <sup>+</sup> -Ph- r, p-(CH3)3-N <sup>+</sup> - CH2CH2- (CCH2CH2)2-O- Ph- (CCH2CH2)2-O- Ph- (CCH2CH2)2-O- Ph- r, p-(N,N-dimethyl- piperazine)-(N')- CH2- CH2-CH2-Ph- piperazine)-(N')- CH2- CH2-CH2-Ph- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph- (OCH2CH2)2-O- Ph- m-CH3O-Ph- 3-4,dioxymethylene-Ph- m-CH3O-P-Ph- 1-p-yridine N-methyl-1-pyridinium P-p-ridine N-methyl-1-pyridinium P-p-ridine N-methyl-1-pyridinium P-p-ridine	7-OH 7-OH 7-OCH 7-OCH 3-OCH 3-SOCH 3-
p-HO-Ph- propyl	propyl proyl pcayl pc2H3 pc4- coline) CH <sub>2</sub> CH,CH <sub>3</sub>	p-HO-Ph. m-CH3-DPh. m-CH3-DPh. m-HO-Ph. p-CH3)3-N-Ph. m-H3-Ph. p-H3-Ph. n-H2-Ph. n-H3-Ph. n-H	7-OCH3 7-O(III) 7-SCH3 7-SCH3 7-SOCH3 7-SOCH3 7-SOCH3 7-SOCH3 7-SOCH3 7-SOCH2 7-SOCH3 7-SOCH3 7-SOCH3 7-SOCH3 7-SOCH3 7-SOCH3 7-NHC(13)3.1' 7-
bury)  m-CH3O-Ph- pentyl  p-(CH3)2N-Ph- 2OC2H5  m-(CH3)2N-Ph- p-(CH3)3-N-Ph- [CH2CH3]-N-Ph- I. p-(CH3)3-N-Ph- I. p-(N,N-dimethyl- piperazine)-(N-Ph- I. m-(N,N-dimethyl- piperazine)-(N-Ph- I. m-(N,N-dimethyl- piperazine)-(N-Ph- I. m-(N,N-dimethyl- piperazine)-(N-Ph- I. m-(N,N-dimethyl- piperazine)-(N-Ph- I. m-CH3O-Ph- I. m-CH3O-Ph- I. p-CH3O-Ph- II p-	butyl pOC2H5 pOC4- coline) CH <sub>2</sub> CH <sub>3</sub>	m-CH30-Ph- m-H0-Ph- p-(CH3)2N-Ph- p-(CH3)2N-Ph- m-H2N-Ph- r-p-(CH3)3-N <sup>4</sup> -Ph- l', p-(CH3)3-N <sup>4</sup> -Ph- l', p-(CH3)3-N <sup>4</sup> - CH2CH2- (OCH2CH2)2-O- Ph- l', m-(CH3)3-N <sup>4</sup> - CH2CH2- (OCH2CH2)2-O- Ph- l', p-(N,N-dimethyl- piperazine)-(N <sup>4</sup> )- CH2- (OCH2CH2)2-O- Ph- l', p-(N,N-dimethyl- piperazine)-(N <sup>4</sup> )- CH2- (OCH2CH2)2-O- Ph- l', m-(N,N-dimethyl- piperazine)-(N <sup>4</sup> )- CH2- (OCH2CH2)2-O- Ph- l', m-(N,N-dimethyl- piperazine)-(N <sup>4</sup> )- CH2- (OCH2CH2)2-O- Ph- m-F, p-CH3O-Ph- 3,4,dioxymethylene-Ph m-CH3O-, p-F-Ph- 4-pyridine N-methyl-4-pyridinium, l' p-pyridine	7-O(iso-propyl) 7-O(iso-propyl) 7-SCH3 7-SCH3 7-SCH2H3 7-SO2H3 7-SCH2CH3 7-NHCH3 7-NHCH3 7-NHCH3 7-NHCH3 7-NHCH3(CH3)3,1' 7-NHCO(CH3)3 7-N(CH3)3,1' 7-NHCO(CH3)3 7-N(CH3)3,1' 7-NHCO(CH3) 7-NHCH3(CH3)3 7-NHCCO(CH3) 7-NH-copholia 7-NN-azeridinium, 1' 7-(N)-N-methyl- pyrolidinium, 1' 7-(N)-N-methyl- pyrolidinium, 1' 7-(N)-N' morpholimium, 1' 7-(N)-N' morpholimium, 1' 7-(N)-N' methyl-piperazine 7-(N)-N' methyl-piperazine 7-(N)-N' methyl-piperazinium, 1' 7-(N)-N' methyl-piperazinium, 1' 7-(N)-N' methyl-piperazinium, 1' 7-(N)-N' methyl-piperazinium, 1' 7-(N)-N' methyl-piperazinium, 1' 7-(N)-N' methyl-piperazinium, 1' 7-(N)-N' MmCO(CH3)B1 7-NH-CO(CH3)B1 7-NH-CO(CH3)B1 7-NH-CO(CH3)B1 7-NH-CO(CH3)B1 7-NH-CO(CH3)B1 7-NH-CO(CH3)B1 8-ethyl 8-eth
m-HO-Ph- pCC2HS pCC2HS pC(H3),N-Ph- pC(H3),N-Ph- pC(H3),N-Ph- p-H3N-Ph- p-H3N-Ph- r, p-(CH3),3-N <sup>+</sup> -Ph- r, p-(CH3),3-N <sup>+</sup> -Ph- r, p-(CH3),3-N <sup>+</sup> -Ph- r, p-(CH3),3-N <sup>+</sup> - r, p-(CH3),3-N <sup>+</sup> - r, p-(CH3),3-N <sup>+</sup> - r, p-(CH3),3-N <sup>+</sup> - r, p-(CH3),3-N <sup>+</sup> - r, p-(CH3),3-N <sup>+</sup> - r, p-(CH2CH2),2-O- ph- r, m-(N,N-dimethyl- piperazine)-(N')- r, p-(N,N-dimethyl- piperazine)-(N')- r, p-(N,N-dimethyl- piperazine)-(N')- r, p-r- ph- m-r, p-r-p- 3-doing-m-r, p-r-ph- 4-pyridine N-methyl-4-pyridinium, r 1- p-r- p-r- p-r- p-r- 1- pyridine N-methyl-3-pyridinium, r 1- p-r- 1-	penyl pC2H3 pC4- coline) CH,CH,	m-HO-Ph- p-(CH <sub>3</sub> ) <sub>2</sub> N-Ph- m-(CH <sub>3</sub> ) <sub>2</sub> N-Ph- p-H <sub>3</sub> N-Ph- r, m-(CH <sub>3</sub> ) <sub>3</sub> N+Ph- r, m-(CH <sub>3</sub> ) <sub>3</sub> N+ CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> C- Ph- (CCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- (CCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- (CCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- (CCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- (CH <sub>2</sub> O- <sub>2</sub> P-F-Ph- 3,4,dioxymethylene-Ph m-CH <sub>3</sub> O- <sub>2</sub> P-F-Ph- 4-pyridine N-methyl-4-pyridinium r P- 2-pyridine	7-SCH3 7-SCH2H3 7-SO2CH3 7-SCH2CH3 7-SCH2CH3 7-SCH2CH3 7-NHCH3 7-NH-Eddinium, I' 7-(N)-N-methyl- pyrrolidinium, I' 7-(N)-N-M-CH3 7-NH-CH3 7-NH-CH3 7-NH-CH3 7-NH-CH3 7-NH-CONC3H1 7-NH-CONC3H1 7-NH-CONC3H1 7-NH-CONC3H2 8-methyl 8-ethyl 8-et
p-(CH <sub>3</sub> ) <sub>2</sub> N-Ph- pol(-4) ——(CH <sub>3</sub> ) <sub>2</sub> N-Ph- pol(-4) ——(CH <sub>3</sub> ) <sub>3</sub> N-Ph- pol(-4) ——(CH <sub>3</sub> ) <sub>3</sub> -N <sup>+</sup> -Ph- I. p-(CH <sub>3</sub> ) <sub>3</sub> -N <sup>+</sup> -Ph- I. p-(CH <sub>3</sub> ) <sub>3</sub> -N <sup>+</sup> -Ph- I. p-(CH <sub>3</sub> ) <sub>3</sub> -N <sup>+</sup> - CH <sub>2</sub> CH <sub>2</sub> ) ——(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- I. m-(CH <sub>3</sub> ) <sub>3</sub> -N <sup>+</sup> - CH <sub>2</sub> CH <sub>2</sub> ) ——(OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- I. p-(N,N-dimethyl- piperazine)-(N')- CH <sub>2</sub> - (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- I. m-(N,N-dimethyl- piperazine)-(N')- CH <sub>2</sub> - (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- I. m-(N,N-dimethyl- piperazine)-(N')- CH <sub>2</sub> - (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph- I. m-(CH <sub>3</sub> O-Ph- J. dioxymethylene-Ph m-CH <sub>3</sub> O <sub>2</sub> -P-Ph- 4-pyridine N-methyl-4-pyridinium, I. 2-pyridine N-methyl-2-yl thienyl-2-yl	20C2H3 20C(4. CH <sub>2</sub> CH <sub>3</sub>	P(CH3)2N-Ph. p-(CH3)2N-Ph. p-(CH3)3-N+2Ph. p-(CH3)3-N+2Ph. r, p-(CH3)3-N+2Ph. r, p-(CH3)3-N+2Ph. r, p-(CH3)3-N+2Ph. r, p-(CH3)3-N+2Ph. r, p-(CH3)3-N+2Ph. r, p-(N,N-dimethyl- piperazine)-(N')- CH2CH2 (OCH2CH2)2-O- Ph. (OCH2CH2)2-O- Ph. (OCH2CH2)2-O- Ph. r, p-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph. r, p-(CH3)3-Ph- 3-A, dioxymethyl-ne-Ph m-CH3O-, p-F-Ph- n-CH3O-, p-F-Ph- 4-pyridine N-methyl-4-pyridinium r 3-pyridine N-methyl-3-pyridinium r 3-pyridine	7-SOCH3 7-SOCH3 7-SOCH3 7-SOCH3 7-SOCH3 7-SOCH3 7-SOCH2 7-NHOH 7-NHC(H3)3, I' 7-NHC(H3)3, I' 7-NHC(O)CH3 7-N(CH2)CH3 7-N(CH2)CH3 7-N(CH3)CH3 7-N(CH3)CH3 7-N(CH3)CH3 7-N(CH3)CH3 7-N(CH3)CH3 7-NN-ECH3 7-NN-ECH3 7-NN-ECH3 7-NN-ECH3 7-NN-ECH3 7-NN-ECH3 7-NN-ECH3 7-NN-COCH3 8-methyl 8-ethyl
20-(4- p-(2-13)2N-Ph- coline) p-12N-Ph- m-12N-Ph- m-12N-Ph- I', p-(CH3)3-N <sup>+</sup> -Ph- I', p-(CH3)3-N <sup>+</sup> - CH2(H2)3-N <sup>+</sup> - CH2(H2)3-N <sup>+</sup> - CH2(H2) I', p-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2(CH2)2-O- Ph- I', m-(N,N-dimethyl- piperazine)-(N')- CH2- CH3(ON)- I', m-(N,N-dimethyl- piperazine)-(N')- CH2- CH2(H2)- I', m-(N,N-dimethyl- I', m-(N,N-dim	20-(4- coline) CH <sub>2</sub> CH <sub>3</sub>	m-(CH3)2N-Ph- p-H3N-Ph- m-H2N-Ph- m-H2N-Ph- n-H2N-Ph- r, p-(CH3)3-N*-Ph- r, p-(CH3)3-N*- CH2CH2)2-O- Ph- r, m-(CH3)3-N*- CH2CH2)2-O- Ph- r, m-(CH3)3-N*- CH2CH2)2-O- Ph- r, p-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph- r, m-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph- r, m-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph- m-F, p-CH3O-Ph- m-F, p-CH3O-Ph- m-F, p-CH3O-Ph- 3.4,dioxymethylene-Ph m-CH3O-, p-F-Ph- 4-pyridine N-methyl-4-pyridinium r 3-pyridine N-methyl-4-pyridinium r 3-pyridine	7-SO2CH3 7-SCH2CH3 7-SCH2CH3 7-NHOH 7-NHCH3 7-NHCH3 7-NHC(GH3)3, 1" 7-NHC(O)CH3 7-N(CH2)13 7-N(CH2)CO2H 7-N*(Me)2CH2CO2H, 1" 7-(N)-morpholine 7-(N)-N-methyl- prolidinium, 1" 7-(N)-Writidinium, 1" 7-(N)-N-methyl- prolidinium,
ooline)  p-H2N-Ph. (CH <sub>3</sub> CH <sub>4</sub> )  r. p-(CH <sub>3</sub> )3-N <sup>4</sup> -Ph. r. p-(CH <sub>3</sub> )3-N <sup>4</sup> -Ph. r. m-(CH <sub>3</sub> )3-N <sup>4</sup> -Ph. r. p-(CH <sub>3</sub> )3-N <sup>4</sup> - CH <sub>2</sub> CH <sub>2</sub> - (OCH <sub>2</sub> CH <sub>2</sub> )2-O- Ph. r. m-(CH <sub>3</sub> )3-N <sup>4</sup> - CH <sub>2</sub> CH <sub>2</sub> - (OCH <sub>2</sub> CH <sub>2</sub> )2-O- Ph. r. p-(N,N-dimethyl- piperazine)-(N')- CH <sub>2</sub> - (OCH <sub>2</sub> CH <sub>2</sub> )2-O- Ph. r. m-(N,N-dimethyl- piperazine)-(N')- CH <sub>2</sub> - (OCH <sub>2</sub> CH <sub>2</sub> )2-O- Ph. r. m-(N,N-dimethyl- piperazine)-(N')- CH <sub>2</sub> - (OCH <sub>2</sub> CH <sub>2</sub> )2-O- Ph. m-F, p-CH <sub>3</sub> O-p-F-Ph- 3-4,dioxymethylene-Ph m-CH <sub>3</sub> O <sub>3</sub> , p-F-Ph- 4-pyridine N-methyl-4-pyridinium, r. 3-pyridine N-methyl-2-yl 5-Cl-thienyl-2-yl 5-Cl-thienyl-2-yl	ch,ch,	p-H3N-Ph. n-H2N-Ph. l', p-(CH3)3-N <sup>+</sup> -Ph. l', p-(CH3)3-N <sup>+</sup> -Ph. l', m-(CH3)3-N <sup>+</sup> - (OCH2CH2)2-O- Ph. l', m-(CH3)3-N <sup>+</sup> - (OCH2CH2)2-O- Ph. l', p-(N,N-dimethyl- piperazino-(N')- CH2- (OCH2CH2)2-O- Ph. l', p-(N,N-dimethyl- piperazino-(N')- CH2- (OCH2CH2)2-O- Ph. l', m-(N,N-dimethyl- piperazino-(N')- CH2- (OCH2CH2)2-O- Ph. l', m-(N,N-dimethyl- piperazino-(N')- CH2- (OCH2CH2)2-O- Ph. m-F, p-CH3O-Ph- 3,4,dioxymethylene-Ph m-CH3O-, p-F-Ph- 4-pyridine N-methyl-4-pyridinium, l' p-pridine N-methyl-4-pyridinium, l' p-pridine N-methyl-3-pyridinium, l' p-pridine N-methyl-3-pyridinium, l' p-pyridine	7-SCH2CH3 7-NH2 7-NH2 7-NHCH3 7-NHCH3 7-NHC(CH3)3, 1' 7-NHC(O)CH3 7-NHC(CH2)3, 1' 7-NHC(O)CH3 7-NHC(CH2)2 7-NMcCH2CO2H 7-NHCH3)2 7-NMcCH2CO2H 7-NH-CO2H 7-NH-corpholine 7-(N)-azeridinium, 1' 7-(N)-pytrolidinium, 1' 7-(N)-N-methyl- pytrolidinium, 1' 7-(N)-N-methyl- pytrolidinium, 1' 7-(N)-N-methyl- pytrolidinium, 1' 7-(N)-N' morpholimium, 1' 7-(N)-N' - methylipierazini 7-(N)-N' - methylipierazinium, 1' 7-(N)-N' - methylipierazinium, 1' 7-(N)-N' - methylipierazinium, 1' 7-(N)-N' - methylipierazinium, 1' 7-(N)-N' - methylipierazinium, 1' 7-(N)-N' - MincHylipierazinium, 1' - 1-(N)-N' MincHylipierazinium, 1'
CH <sub>3</sub> CH <sub>3</sub> m-H <sub>2</sub> N-P <sub>b</sub> 1, p-(CH <sub>3</sub> )3-N <sup>4</sup> -P <sub>b</sub> .  1, p-(CH <sub>3</sub> )3-N <sup>4</sup> -P <sub>b</sub> .  1, p-(CH <sub>3</sub> )3-N <sup>4</sup> -  CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> C-  P <sub>b</sub> (CH <sub>2</sub> CH <sub>2</sub> )2-O- P <sub>b</sub> 1, m-(CH <sub>3</sub> )3-N <sup>4</sup> -  CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> C-  (CH <sub>2</sub> CH <sub>2</sub> )2-O- P <sub>b</sub> 1, p-(N <sub>1</sub> N-dimethyl- piperazine)-(N')-  CH <sub>2</sub> (OCH <sub>2</sub> CH <sub>2</sub> )2-O- P <sub>b</sub> 1, m-(N <sub>1</sub> N-dimethyl- piperazine)-(N')-  CH <sub>2</sub> (OCH <sub>2</sub> CH <sub>2</sub> )2-O- P <sub>b</sub> 1, m-(N <sub>1</sub> N-dimethyl- piperazine)-(N')-  CH <sub>2</sub> (OCH <sub>2</sub> CH <sub>2</sub> )2-O- P <sub>b</sub> 1, m-CH <sub>3</sub> O-P <sub>b</sub> 3-4 dioxymethyl-ne-Ph m-CH <sub>3</sub> O <sub>2</sub> -P-P <sub>b</sub> 4-pyridine N-methyl-3-pyridinium, 1 2-pyridine N-methyl-2-yl 5-Cl-thiemyl-2-yl 5-Cl-thiemyl-2-yl 5-Cl-thiemyl-2-yl	CH;CH;	m-H <sub>2</sub> N-Ph. Ir, p-(CH <sub>3</sub> ) <sub>3</sub> -N <sup>+</sup> -Ph. Ir, p-(CH <sub>3</sub> ) <sub>3</sub> -N <sup>+</sup> -Ph. Ir, p-(CH <sub>3</sub> ) <sub>3</sub> -N <sup>+</sup> -Ph. Ir, p-(CH <sub>3</sub> ) <sub>3</sub> -N <sup>+</sup> - CH <sub>2</sub> CH <sub>2</sub> . OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph. OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph. Ir, p-(N,N-dimethyl- piperazine)-(N')- CH <sub>2</sub> - CH <sub>2</sub> - CH <sub>2</sub> - CH <sub>2</sub> - CH <sub>2</sub> - CH <sub>2</sub> - CH <sub>2</sub> - Ph. OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph. OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph. OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph. OCH <sub>2</sub> CH <sub>2</sub> D- Ph. OCH <sub>3</sub> O- Ph- DCH <sub>3</sub> O- Ph- D- A, dioxymethylene-Ph m-CH <sub>3</sub> O- Ph- p-ridine N-methyl-4-pyridinium P- p-pridine N-methyl-3-pyridinium P- P- P- P- P- P- P- P- P- P- P- P- P-	7-NH2 7-NHCH3 7-NHCH3 7-NHCH3 7-NHCH3]3, 1° 7-NHC(CH3)3, 1° 7-NHC(CH2)CH3 7-NHC(CH2)CH3 7-NHCCH2CO2H, 7-NHCCH2CO2H, 7-NH-MeCH2CO2H, 7-NH-Mech2CH2CO2H, 7-NH-Mech3-Mech2CH3CO2H, 7-NH-Mech3
I', p-(CH3)3-N <sup>+</sup> .Ph. I', m-(CH3)3-N <sup>+</sup> . CH2CH2-CH2)2-O. Ph. I', m-(CH3)3-N <sup>+</sup> . CH2CH2-CH2)2-O. Ph. I', m-(CH3)3-N <sup>+</sup> . CH2CH2-CH2)2-O. Ph. I', p-(N,N-dimethyl-piperazine)-(N')-CH2-CH2)2-O. Ph. I', m-(N,N-dimethyl-piperazine)-(N')-CH2-CH2)2-O. Ph. I', m-(N,N-dimethyl-piperazine)-(N')-CH2-CH2)2-O. Ph. I', m-(N,N-dimethyl-piperazine)-(N')-CH2-CH2)2-O. Ph. I', m-(N,N-dimethyl-Ph-3-4,dioxymethylene-Ph-3-4,dioxymethylene-Ph-3-4,dioxymethylene-Ph-3-4,dioxymethylene-Ph-3-pyridine N-methyl-4-pyridinium, I' I'-pyridine N-methyl-3-pyridinium, I'-pyridine N-methyl-3-pyridinium, I'-pyridine N-methyl-2-yl S-Cl-thiemyl-2-yl S-Cl-thiemyl-2-yl		1. p-(CH3)3-N <sup>+</sup> . ph. 1. m-(CH3)3-N <sup>+</sup> . ph. 1. m-(CH3)3-N <sup>+</sup> . CH2(H3)3-N <sup>+</sup> . CH2(H2)2-O- ph. 1. m-(CH3)3-N <sup>+</sup> . CH2(H2)2-O- ph. 1. p-(N,N-dimethyl- piperazine)-(N')- CH2. (OCH2(CH2)2-O- ph. (OCH2(CH2)2-O-	7.NHOH 7.NHOH 7.NHC(H <sub>3</sub> ) 7.N(CH <sub>2</sub> ) 7.N'(CH <sub>3</sub> ) 7.N'(CH <sub>3</sub> ) 7.N'(CH <sub>3</sub> ) 7.N(CH <sub>2</sub> CH <sub>3</sub> ) 7.N'(Me) <sub>2</sub> CH <sub>2</sub> CO <sub>2</sub> H 7.N'(Me) <sub>2</sub> CH <sub>3</sub> CO <sub>2</sub> H 7.N'-Me 7.N)-morpholine 7.(N)-width 7.(N)-Width 7.(N)-Width 7.(N)-Width 7.(N)-Width 7.(N)-N-methyl- morpholinium, I' 7.(N)- N-methyl- morpholinium, I' 7.(N)- N-methyl- 7.NH-CN-N' methylipierazinium, I' 7.NH-CBZ 7.NH-CONC3H <sub>1</sub> 7.NH-CONC3H <sub>1</sub> 7.NH-CONC3H <sub>1</sub> 7.NH-CONC3H <sub>2</sub> 8.methyl 8.eibyl
I', m-(CH3)3-N*-Ph- I', p-(CH3)3-N*- CH2CH2)-O- Ph- I', m-(CH2)3-N*- CH2CH2)2-O- Ph- I', p-(N,N-dimethyl- piperazine)-(N')- CH2- (CCH2CH2)2-O- Ph- I', m-(N,N-dimethyl- Ph- I', m-(N,N-dimethyl- Ph- I', m-(N,N-dimethyl- Ph- I', m-(N,N-dimethyl- Ph- I', m-(N,N-dimethyl- Ph- I', m-(N,N-dimethyl- I', m-(N,N-dimethyl-I') I', m-(N,N-dimethyl-I') I', m-(N,N-dimethyl-I') I', m-(N,N-dimethyl-I') I', m-(N,N-dimethyl-I') I', m-(N,N-dimethyl-I') I', m-(N,N-dimethyl-I') I', m-(N,N-dimethyl-I') I', m-(N,N-dimethyl-I') I', m-(N,N-dimethyl-I') I', m-(N,N-dimethyl-I') I', m-(N,N-dimethyl-I') I', p-(N,N-dimethyl-I') I', p-(		I', m-(CH3)3-N <sup>+</sup> -Ph- I', p-(CH3)3-N <sup>+</sup> . CH2CH2)2-O- Ph- I', m-(CH3)3-N <sup>+</sup> . CH2CH2, COCH2CH2)2-O- Ph- I', p-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph- I', m-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph- I', m-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph- m-F, p-CH3O-Ph- m-GH3O-, p-F-Ph- m-CH3O-, p-F-Ph- 4-pyridine N-methyl-4-pyridinium, I' 3-pyridine N-methyl-3-pyridinium, I' 2-pyridine	7-NHCH3 7-N(CH3)3, I' 7-N(CH3)3, I' 7-N(CH2)3, I' 7-NHC(O)CH3 7-N(CH2CH3)2 7-NMeCH2CO2H 7-N'(Me)2CH2CO2H 7-N'(Me)2CH2CO2H 7-N'-Mech2CH2CO2H 7-N'-Mech2CH2CO2H 7-(N)-azeridine 7-(N)-azeridine 7-(N)-N-methyl- pyrrolidinium, I' 7-(N)- N-methyl- N-methyl- pyrrolidin
+.  12)2-0.  12)2-0.  12)2-0.  12)2-0.  12)2-0.  12)2-0.  12)2-0.  12)2-0.  12)2-0.  14  1dinium,  1dinium,	r, p-(CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> - (OC) Ph. r, m-(CH CH <sub>2</sub> CH <sub>2</sub> - (OC) Ph. r, p-(N,N) pipe CH <sub>2</sub> - (OC) Ph. r, m-(N,N) pipe CH <sub>2</sub> - (OC) Ph. r-F, p-CH 3,4,dioxyn m-CH <sub>3</sub> O <sub>2</sub> O 4-pyridine N-methyl- r 2-pyridine N-methyl- r 2-pyridine p-CH <sub>3</sub> O <sub>2</sub> O thienyl-2-2 chienyl-2-2 chi	I', p-(CH3)3-N <sup>+</sup> . CH2CH2)-C-Ph I', m-(CH3)3-N <sup>+</sup> . CH2CH2, CH2CH2)-C-Ph I', p-(N,N-dimethyl-piperazine)-(N')- CH2. CH2CH2)-C-Ph I', m-(N,N-dimethyl-piperazine)-(N')- CH2. COCH2CH2)2-C-Ph I', m-(N,N-dimethyl-piperazine)-(N')- CH2. CH2-CH3C-Ph I', m-(N,N-dimethyl-piperazine)-(N')- CH2-CH3C-Ph I', m-(N,N-dimethyl-piperazine)-(N')- CH2-CH3C-Ph I', m-(N,N-dimethyl-piperazine)-(N')- CH2-CH3C-Ph I', m-(N,N-dimethyl-piperazine)-(N')- CH2-CH3C-Ph I', p-CH3C-Ph I', p-CH	7-N(CH3)) 7-N(CH3)), I' 7-N'C(CH3)), I' 7-N'C(CH2)CH3 7-N'CCH2CO2H 7-N'H(Me)2CH2CO2H, I' 7-(N)-azeridine 7-(N)-azeridine 7-(N)-v-methyl- pyrolidinium, I' 7-(N)- N-methyl- morpholimium, I' 7-(N)- N-methyl- pyrolidinium, I' 7-(N)- N-methyl- pyrolidinium, I' 7-(N)- N-methyl- pyrolidinium, I' 7-(N)- N-methyl- pyrolidinium, I' 7-(N)- N-methyl-piperazine 7-(N)-N'.  methyl-piperazinium, I' 7-(N)-N'.  methyl-piperazinium, I' 7-(N)-N'.  dimethyl-piperazinium, I' 7-NH-CBZ  7-NH-CBZ  7-NH-CO)C3H11  7-NH-CO)C3H11  7-NH-CO)C3H11  7-NH-CO)CH2BT  7-NH-CONCH2BT  7-NH-CONCH2BT  7-NH-CONCH2BT  7-NH-CONCH2BT  7-NH-CONCH2BT  7-NH-CONCH2BT  7-NH-CONCH2BT  7-NH-CONCH2BT  7-NH-CONCH2BT  8-methyl  8-sto-propyl  8-sto-propyl
12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 14dinium, 1dinium,	CH2CH2  Ph (OCI Ph CH2CH2 (OCI Ph CH2CH2 (OCI Ph CH2CH2 (OCI Ph CH2 (OCI Ph CH2 (OCI Ph CH2 (OCI Ph CH2 (OCI Ph T, m-(N,N Pipes CH2 (OCI Ph T, m-(N,N Pipes CH2 (OCI Ph T- p-CH3 J-4/diov, T- cH3 J-pyridian N-methyl-1 T P-CH3O2( thienyl-2-2 S-CI-thiem S-CI-thiem	CH2CH2	7.N <sup>1</sup> (CH3)3, I' 7.NHC(O)CH3 7.NHC(O)CH3 7.NCH2(GH3)2 7.NMcCH3;CO <sub>2</sub> H 7.N <sup>1</sup> (Me)2CH2CO <sub>2</sub> H 7.N <sup>1</sup> (Me)2CH2CO <sub>2</sub> H 7.N <sup>1</sup> (Me)2CH3CO <sub>2</sub> H 7.N <sup>1</sup> (N)-morpholine 7.(N)-N-methyl- pyrrolidinium, I' 7.(N)-N-methyl- pyrrolidinium, I' 7.(N)-N-methyl- propholinium, I' 7.(N)-N' morpholinium, I' 7.(N)-N' methylipierazinium 7.(N)-N' dinethylipierazinium, I' 7.NH-CBZ 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br 7.NH-CO(C)H <sub>2</sub> Br
12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 13)2-0- 14inium,	Ph. (OC) Ph. (CH2CH2- CH2CH2- CH2CH2- COC) Ph. (CC) Ph. (CH2- CH2- (OC) Ph. (CH2- (OC) Ph. (O	Ph. CH2CH2)2-O-Ph. T. m.(CH3)3-N <sup>+</sup> . CH2CH2; Ph. CH2CH2; Ph. CH2CH2)2-O-Ph. CH2-CH2)2-O-Ph. T. m.(N.N-dimethyl-piperazine)-(N')-CH2- CH2-CH2-CH2)2-O-Ph. T. m.(N.N-dimethyl-piperazine)-(N')-CH2- CH2-CH2-CH2)2-O-Ph. T. p.CH3O-Ph. T. p.CH3O-Ph. 3.4,dioxymethylene-Ph. m.F. p.CH3O-p.F-Ph. MCH3O-y. p.F-Ph. 4.pyridine N-methyl-4-pyridinium, T. p.Pridine N-methyl-3-pyridinium, T. p.Pridine N-methyl-3-pyridinium, T. p.Pridine	7.NHC(O)CH3 7.NHC(O)CH3 7.N(CH2CH3)2 7.N(CH2CH3)2 7.N(CH2CH3)2 7.NM-morpholine 7.(N)-morpholine 7.(N)-pyrrolidine 7.(N)-t-methyl- methylazeridinium, I * 7.(N)- pyrrolidinium, I * 7.(N)- morpholinium, I * 7.(N)- N-methyl- pyrrolidinium, I * 7.(N)- Morpholinium, I * 7.(N)-N'- dimethylpiperazine 7.(N)-N'- dimethylpiperazinium, I * 7.NH-CO)CSHII 7.NH-CONSHIII 7.NH-C
ft. ft. f2)2-0. f2)2-0. f2)2-0. f2)2-0. f2)2-0. f2)2-0. f2)2-0. f2)2-0. f3)2-0. f3)2-0. f3)2-0. f4 fdinium,	Ph- IT, m-(CH CH2CH2- Ph- IT, p-(N,N IT, p-(N,N IT, m-(N,N  IT, m-(N,N IT, m-(N,N) IT, m-(N,N IT, m-(N,N) IT, m-(N,N) IT, m-(N,N) IT, m-(N,N) IT, m-(N,N) IT, m-(N,N) IT, m-(N,N,N) IT, m-(N,N)	Ph. I', m-(CH3)3-N". CH2CH2; C(OCH2CH2)2-O. Ph. I', p-(N,N-dimethyl- piperazine)-(N')- CH2: (OCH2CH2)2-O. Ph. I', m-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O. Ph. m-F, p-CH3O-Ph. m-F, p-CH3O-Ph. m-F, p-CH3O-Ph- m-CH3O-, p-F-Ph. 4-pyridine N-methyl-4-pyridinium, 1- pyridine N-methyl-3-pyridinium, 1- pyridine N-methyl-3-pyridinium, 1- pyridine	7-N(CH2CH3)2 7-NMcCH2CO2H 7-NMcCH2CO2H 7-NMcCH2CO2H 7-NM-CH2CO2H 7-NN-morpholine 7-(N)-acridine 7-(N)-N-methylacridinim, I' 7-(N)-pyrrolidinium, I' 7-(N)-pyrrolidinium, I' 7-(N)-N-methyl-pyrrolidinium, I' 7-(N)-N-methyl- morpholinium, I' 7-(N)-N-M-CH3-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-N-M-CN-M-M-CN-M-CN-M-CN-M-CN-M-CN-M-CN-M-CN-M-CN-M-M-CN-M-M-CN-M-M-CN-M-M-M-M
7†. 2))2-0- 2))2-0- 2))2-0- 2))2-0- 2))2-0- 2))2-0- 2))2-0- 2))2-0- 2) 4 dimium,	CH2CH2C CH2CH2CH2CH2CH2CH2CH2CH2CH2CH2CH2CH2CH2C	T. m(CH3)3-N <sup>+</sup> . CH2CH2; C(CCH2CH2)2-O- Ph- T. p-(N,N-dimethyl- piperazino-(N')- CH2; (OCH2CH2)2-O- Ph- T. m-(N,N-dimethyl- piperazine)-(N')- CH2; (OCH2CH2)2-O- Ph- CH2- (OCH2CH2)2-O- Ph- m-T, p-CH3O-Ph- 3,4,dioxymethylene-Ph m-CH3O, p-F-Ph- 4-pyridine N-methyl-4-pyridinium, T- 2-pyridine N-methyl-3-pyridinium, T- 2-pyridine	7-NMcCH2CO2H 7-NMcCH2CO2H 7-NMCH2CO2H, 1-NM-corpholine 7-(N)-azetidine 7-(N)-N-methyl- methylazetidinium, I-7-(N)- N-methyl- pyrrolidinium, I-7-(N)- N-methyl- morpholinium, I-7-(N)- N-methyl- morpholinium, I-7-(N)- N-methylpiperazine 7-(N)-N' methylpiperazinium, I-7-(N)-N' - Minethylpiperazinium, I-7-NH-CO2H2B1 7-NH-CO2H2B1 7-NH-CO3H11 8-NH-CO3H11 8-NH-CO3H11 8-NH-CO3H11 8-NH-CO3H11 8-NH-CO3H11 8-NH-CO3H11 8-NH-CO3H11 8-NH-CO3H11 8-NH-CO3H11 8-NH
12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 14 1dinium, 1dinium,	CH2CH2- Ph- (OCI Ph- (OCI Ph- (T, m-(N,N Piper CH2- (OC) Ph- m-F, p-CH 3,4 doxyn m-CH30-0,4-pyridine N-methyl-1- 1 2-pyridine P-CH302(thienyl-2-) 5-Cl-thieny	CH2CH2. (CCH2CH2)2-O- Ph (CCH2CH2)2-O- Ph (CCH2CH2)2-O- Ph (CCH2CH2)2-O- Ph (CCH2CH2)2-O- Ph (CCH2CH2)2-O- Ph (CCH2CH2)2-O- Ph (CCH2CH2)2-O- Ph (CCH2CH2)2-O- Ph (CCH2CH2)2-O- Ph (CCH2CH2)2-O- Ph (CCH2CH2)2-O- Ph (CCH2CH2)2-O- Ph (CCH2CH2)2-O- Ph (CH2CH2O-Ph (CCH2CH2)2-O- Ph (CH2CH2)2-Ph (CH2CH2)3-Ph (CH3O-PF-Ph 4-Apridiane N-methyl-4-pyridinium 1- Pyridiane N-methyl-3-pyridinium 1- Pyridiane 1- Pyridiane	7-N+f(Me)2CH2CO2H, 1 1 1 1-QN)-morpholine 7-(N)-azeridime 7-(N)-yvareidimim, I '7-(N)-pyrrolidimim, I '7-(N)-N-methyl- pyrrolidimium, I '7-(N)-N-methyl- morpholimium, I '7-(N)-N'- morpholimium, I '7-(N)-N'- methyl-pierazine 7-(N)-N'- methyl-pierazinium, I '7-NH-CBZ 7-NH-CONC3H11 7-NH-CONC3H11 7-NH-CONC3H21 7-NH-CONC3H2Br 7-NH-CONCH2Br 8-methyl 8-ethyl
12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 14inium, 14inium,	(OC) Ph. 17, p-(N,N) pipe CH2- (OC) Ph. 17, m-(N,N) 17, m-(N,N) 18, m-F, p-CH 19, d-dioxy 18, d-dioxy 18, d-dioxy 19, d-dioxy	(OCH2CH2)2-O-Ph-Ph-Ph-Ph-Ph-Ph-Ph-Ph-Ph-Ph-Ph-Ph-Ph-	7-(N)-morpholine 7-(N)-azeridine 7-(N)-N: methylazeridinium, I' 7- (N)-pyrolidinium, I' 7- (N)-N-methyl- pyrolidinium, I' 7-(N)- N-methyl- morpholinium, I' 7-(N)- N-methyl- morpholinium, I' 7-(N)-N': methylpiperazinium 7-(N)-N': dimethylpiperazinium, I' 7-NH-CBZ 7-NH-CONC3H11 7-NH-CONC3H21 7-NH-CONC3H21 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONT)NH2 7-(2)-thiophene 8-methyl 8-eibyl 8-eibyl 8-eibyl 8-eibyl 8-eibyl
thyl- 12)2-O- 12)2-O- 12)2-O- 12)2-O- 12)2-O- 14 1dinium, idinium,	Pb. I'. p-(N,N pipe) CH2. (OCI Ph. (OCI Ph. I'. m-(N,N I'. m-(N,N I'. m-(N,N Pipe) CH2. (OCI Ph. III. m-F, p-CH 3,4,dioxyn m-CH3O-4-pyridine N-methyl-I'. I'. 2-pyridine N-methyl-I'. 1-2-pyridine	1, p(N,1-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph- (",m-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph- m-F, p-CH3O-Ph- 3.4,dioxymethyl-en-Ph- m-CH3O-y, p-F-Ph- 4-pyridine 4-pyridine N-methyl-4-pyridinium, 1- 2-pyridine	7-(N)-morpholine 7-(N)-zeridine 7-(N)-zeridine 7-(N)-)-methylazeridinium, I 7-(N)- methylazeridinium, I 7-(N)- pyrrolidinium, I 7-(N)- morpholinium, I 7-(N)- N-methyl- morpholinium, I 7-(N)- N-methyl- morpholinium, I 7-(N)-N'- dimethylpiperazine 7-(N)-N'- dimethylpiperazinium, I 7- NH-COSZ 7-NH-CON-3-BI 7-NH-CON-3-BI 7-NH-CON-3-BI 7-NH-CON-3-BI 8-methyl 8-ethyl 8-ethyl 8-ethyl 8-ethyl 8-ethyl 8-ethyl 8-ethyl 8-ethyl 8-ethyl
thyl- (N'') 12/2-0 12/2-0 12/2-0 12/2-0 12/2-0 12/2-0 14 1dinium, 1dinium,	r; p-(N,N pipe CH2. (OCI Ph 1; m-(N,N pipe CH2. (OCI Ph Addioxyn m-CH30- 4-pyridine N-methyl- 1- 2-pyridine p-CH30-Q thieny1-2- 5-CI-thieny	17. p-(N.N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph- 17. m-(N.N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph- m-F, p-CH3O-Ph- 3.4,dioxymethylene-Ph m-CH3O-, p-F-Ph- 4-pyridine N-methyl-4-pyridinium, 1- p-pyridine N-methyl-3-pyridinium, 1- 2-pyridine	7-(N)-acridine 7-(N)-N- methylaceridinium, I' 7- (N)-pyrrolidine 7-(N)-N-methyl- pyrrolidinium, I' 7-(N)- N-methyl- morpholinium, I' 7-(N)-N' morpholinium, I' 7-(N)-N' morpholinium, I' 7-(N)-N' imethyleperazine 7-(N)-N' imethyleperazinium, I' 7-NH-CBZ 7-NH-CDCH <sub>2</sub> Br 7-NH-COCH <sub>2</sub> NH 8-ethyl 8-ethyl 8-ethyl 8-ethyl 8-ethyl
12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 12)2-0- 13)2-0- 14)2-0	CH2- (OC) Ph- [1, m-(N,N) pipe CH2- pipe CH2- (OC) Ph- M-F, p-CH 3,4 dixyn m-CH3O- 4-pyridine N-methyl- 1- 2-pyridine 2-pridine 2-pridine 2-pridine 2-pridine 2-pridine 2-pridine 2-pridine 2-pridine	piperazine)-(N')- CH2- (CCH2CH2)2-O- Ph. [', m-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph. (OCH2CH2)2-O- Ph. m-CH3O-Ph- 3,4,dioxymethylene-Ph m-CH3O-, p-F-Ph- 4-pyridine N-methyl-4-pyridinium, [' N-methyl-3-pyridinium, I' 2-pyridine	7-(N)-N- methylacidinium, I · 7- (N)-pyrolidine 2-(N)-N-methyl- pyrolidinium, I · 7-(N)- N-methyl- morpholinium, I · 7-(N)-N' morpholinium, I · 7-(N)-N' methyl-pierazini e 7-(N)-N' dimethyl-pierazinium, I · 7-NH-CBZ 7-NH-CONC3H11 7-NH-CONC3H21 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 8-methyl 8-siso-propyl 8-siso-propyl
12)2-O- ethyl	CH2- (OC) Ph. I', m-(N,N pipes CH2- CH2- (OC) Ph- Th- II-, p-CH3- J-pyridine N-methyl- I' P-CH3-O2- CH3-O2- Chienyl-2- S-CI-thiem	CH2- (OCH2CH2)2-O- ph.  I', m-(N,N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- ph.  m-F, p-CH3O-ph- 3/, dioxymethylene-Ph m-CH3O-, p-F-Ph- 4-pyridine N-methyl-4-pyridinium, I' 3-pyridine N-methyl-3-pyridinium, I'	methylazeridinium, I' 7. (N)-pyrolaidinium, I' 7-(N)-N-methyl- pyrrolidinium, I' 7-(N)- N-methyl- morpholinium, I' 7-(N)-N'- methylpiperazinie 7-(N)-N'- dinethylpiperazinium, I' 7-NH-CBZ 7-NH-CONC3H11 7-NH-CONC3H21 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONCH2Br 7-NH-CONT)NH2 8-methyl 8-sebyl 8-sebyl 8-sebyl
12)2-0- 12)2-0	Ph. I'. m-(N,N) I'. m-(N,N) I'. m-(N,N) I'. m-(N,N) I'. m-(N,N) I'. m-(N,N) I'. m-(N,N) I'. m-(H,2O) I'. m-(H	(OCH2CH2)2-O- Ph. I', m-(N.N-dimethyl- piperazine)-(N')- CH2- (OCH2CH2)2-O- Ph. m-F, p-CH3O-Ph- 3.4,dioxymethylene-Ph m-CH3O-y. p-F-Ph- 4-pyridine N-methyl-4-pyridinium, 1-pyridine N-methyl-3-pyridinium, I'	(N)-pyrolidine 7-(N)-N-methyl- pyrolidinium, I' 7-(N)- N-methyl- morpholinium, I' 7-(N)-N'- methylpiperazine 7-(N)-N'- dimethylpiperazinium, I' 7-NH-COS4H1 7-NH-COS5H11 7-NH-C(NH)NH2 7-(Y)-thiophene 8-methyl 8-ethyl 8-iso-propyl
tchyl- 1))2-O- 1))2-O- 1))2-O- 1))2-O- 1) 1) 1) 1) 1) 1) 1) 1) 1) 1) 1) 1) 1) 1)	I. m-(N,N I. m-(N,N I. m-(N,N II. m-(N,N II. m-F, p-CH II. m-F, p-CH II. m-F, p-CH II. m-F, p-CH II. m-CH3O- II. l- Pyridine N-methyl- II. l- Pyridine N-methyl- II. l- Pyridine N-methyl- II. l- Pyridine N-methyl- II. l- Pyridine N-methyl- II. l- Pyridine N-methyl- II. l- P-CH3O- II. l- P-CH3O- II. l- P-CH-III. l- III.	1, ru- 1,	/-(N)-+-methyl- pyrrolidinium, I' 7-(N)- N-methyl- morpholinium, I' 7-(N)-N'- methylpiperazine 7-(N)-N'- dimethylpiperazinium, I' 7-NH-COS2 7-NH-COSH <sub>11</sub> 7-NH-CONH <sub>2</sub> Br 7-NH-C(NH)NH <sub>2</sub> 7-(2)-thiophene 8-methyl 8-ethyl 8-iso-propyl
etnyi- †)-(N')- †)-(N')- †)- †)- †)- † † † † † † † † † † † † †	L. m-(N.N. pipel CH2- (OCI Ph. m-F, p-CH 3,4,dtoxyn m-CH3O-, 4-pyridine N-methyl-I- I- 2-pyridine 2-pyridine 2-pcH3O3(c) p-CH3O3(c) p-CH3O3(c) p-CH3O3(c) p-CH3O3(c) p-CH3O3(c) p-CH3O3(c) p-CH3O3(c) p-CH3O3(c) p-CC-thiemyl-2-3	cH <sub>2</sub> , N-dunetnyi- piperazine)-(N')- CH <sub>2</sub> (OCH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> -O- Ph m-F, p-CH <sub>3</sub> O-Ph 3,4,dioxymethylene-Ph m-CH <sub>3</sub> O <sub>2</sub> , p-F-Ph 4-pyridine N-methyl-4-pyridinium, p- 1-pyridine N-methyl-3-pyridinium, 1- 2-pyridine	pyrolidinium, I' 7-(N)- N-methy! morpholinium, I' 7-(N)-N'. methylpiperazine 7-(N)-N'. dimethylpiperazinium, I' 7-NH-CBZ 7-NH-CBZ 7-NH-CONC3HII 7-NH-C(ONC3HII 7-NH-C(ONC)HII 7-NH-C(ONC)HII 7-NH-C(ONC)HII 8-ethyl 8-ethyl 8-iso-propyl 8-iso-propyl
b. Hene-Ph PP. idinium, idinium,	CH2 (OCI Ph m-F, p-CH 3,4,dtoxyn m-CH3O-, 4-pyridine N-methyl- 1 2-pyridine 2-pyridine 2-pCH3O3(c) thienyl-2-3 5-Cl-thieny	CH2- CH2- (OCH2CH2)2-O- Ph m-F, p-CH3O-Ph 3,4,dioxymethylene-Ph m-CH3O-, p-F-Ph 4-pyridine N-methyl-4-pyridinium, 1- 1- 2-pyridine 1- 2-pyridine	morpholinium, I' 7-(N)-N' morpholinium, I' 7-(N)-N' methylpiperazine 7-(N)-N' dimethylpiperazinium, I' 7-NH-CBZ 7-NH-CONC3H11 7-NH-CONC3H11 7-NH-CONH)NH2 7-(2)-thiophene 8-methyl 8-sito-propyl 8-sito-propyl
12)2-O- Pa- Pa- idinium, idinium,	Ph.  m.F., p.CH 3,4dixym 3,4dixym m.CH300, m.CH300, 4-pyridine N-methyl-1- 1- 2-pyridine 2-pyridine 2-pyridine 2-pyridine 2-cH3002( thienyl-2-y 5-CI-thieny	Ph. m-F, p-CH3O-Ph. 3,4,dioxymethylene-Ph. 3,4,dioxymethylene-Ph. m-CH3O-, p-F-Ph. 4-pyridine N-methyl-4-pyridinium, 7-pyridine N-methyl-3-pyridinium, I'	7-(N)-N': methylpiperazine 7-(N)-N': dimethylpiperazinium, I' 7-NH-CBZ 7-NHC(O)C3H11 7-NHC(O)CH2Br 7-NH-C(NH)NH2 7-(1)-thiophene 8-methyl 8-iso-propyl 8-iso-propyl
h. h. lene-Ph Ph. idinium, idinium,	Ph- m.F. p.CH 3,4diov,n m.CH300,v m.CH300,4-pyridine N.methyl-1 1 2-pyridine N-methyl-1 1 2-pyridine 2-pidine 2-pidine 2-pidine 2-cH3020; thienyl-2-y 5-Cl-thieny	Ph. m-F, p-CH3O-Ph. 3,4,dioxymethylene-Ph m-CH3O-p-F-Ph. 4-pyridine N-methyl-4-pyridinium, 1-pyridine N-methyl-3-pyridinium, I' 2-pyridine	methylpiperazine 7-(N)-N'. dinethylpiperazinium, I' 7-NH-CBZ 7-NHC(O)C5H11 7-NHC(O)CH2Br 7-NH-C(NH)NH2 7-(Y)-thiophene 8-methyl 8-thyl 8-iso-propyl
h, lene-Ph Ph. Ph. idinium, idinium,	n.F. p.CH 3,4,dioxyn n.CH3O- 4-pyridine N-methyl- 1 2-pyridine N-methyl- 1 2-pyridine p-CH3O <sub>2</sub> 5-CI-thieny	m-F, p-CH3O-Ph- 3/4, dioxymethylene-Ph m-CH3O-, p-F-Ph- 4-pyridine 4-pyridine N-methyl-4-pyridinium, 1- 3-pyridine N-methyl-3-pyridinium, 1- 2-pyridine	7-(N)-N': dimethylpiperazinium, I' 7-NH-CBZ 7-NHC(O)C5H11 7-NHC(O)CH2Br 7-NH-C(NH)NH2 7-(1)-thiophene 8-methyl 8-thyl 8-iso-propyl
lene-Ph Ph- idinium, idinium,	n-CH3O- m-CH3O- 4-pyridine N-methyl- I 3-pyridine N-methyl- 1- 2-pyridine p-CH3O <sub>2</sub> O thienyl-2-3- 5-CI-thieny	3.4.dioxymethylene-Ph m-CH3O-, p-F-Ph- 4-pyridine N-methyl-4-pyridinium, P-pyridine N-methyl-3-pyridinium, P-pyridine	dinethylpiperazinium, I- 7-NH-CBZ 7-NHC(O)C5H11 7-NHC(O)CH2Br 7-NH-C(NH)NH2 7-(2)-thiophene 8-methyl 8-ethyl 8-iso-propyl
Ph- idinium, idinium,	n-CH3O, 4-pyridine N-methyl- 1 3-pyridine N-methyl- 1 2-pyridine 2-pyridine 2-filo2( thienyl-2-) 5-Cl-thieny	4-pyridine A-pyridinium, I- N-methyl-4-pyridinium, I- N-methyl-3-pyridinium, I- 2-pyridine	7-NH-COBZ 7-NH-COC5H11 7-NH-COCH2Br 7-NH-C(NH)NH2 7-(2)-thiophene 8-methyl 8-ethyl 8-iso-propyl
idinium, idinium,	N-methyl- I- 3-pyridine N-methyl- I- 2-pyridine 2-pyridine p-CH <sub>3</sub> O <sub>2</sub> C thienyl-2-3	N-methyl-4-pyridinium, I' 3-pyridine N-methyl-3-pyridinium, I'	NHC(O)C;3H[1 NHC(O)CH2Br NH-C(NH)NH2 (12)-thiophene methyl 8-methyl 8-thyl 8-iso-propyl
idinium,	N-memyl- 1- 3-pyridine N-methyl- 1- 2-pyridine p-CH3O30 bitmyl-2-3 5-Cl-thiemy	N-methyl-4-pyridinium, 1 3-pyridine N-methyl-3-pyridinium, 1 2-pyridine	7-NHC(O)CH2Br 7-NH-C(NH)NH2 7-(2)-thiophene 8-methyl 8-ethyl 8-iso-propyl
idinium,	3-pyridine N-methyl-1 1- 2-pyridine p-CH3O2( thienyl-2-) 5-Cl-thien	3-pyridine N-methyl-3-pyridinium, I	7-(1)-thiophene 7-(2)-thiophene 8-methyl 8-ethyl 8-iso-propyl
idinium,	N-methyl- 1- 2-pyridiae p-CH3026 thienyl-2-3 5-Cl-thieny	N-methyl-3-pyridinium, I' 2-pyridine	7-(2)-thiophene 8-methyl 8-ethyl 8-iso-propyl
A idinium,	r-metay- l- 2-pyritue p-CH3O2c thienyl-2-3 5-Cl-thieny	N-methyl-3-pyridinium, I* 2-pyridine	8-methyl 8-ethyl 8-iso-propyl
7	2-pyridiae p-CH3O2( thienyl-2-) 5-CI-thien	2-pyridine	8-ethyl 8-iso-propyl
72	2-pyridiae p-CH3O <sub>2</sub> C thienyl-2- <sub>3</sub> 5-CI-thien	2-pyridine	8-iso-propyl
2	p-CH <sub>3</sub> O <sub>2</sub> C thienyl-2-y 5-Cl-thien		
2	thienyl-2-y 5-Cl-thien	P-CH3O2C-Pb-	8-tert-butyl
-2-yl	5-C1-thien	thicnyl-2-yl	HO-8
	_	5-Cl-thienyl-2-yl	8-OCH <sub>3</sub>
		,	

Another class of compounds of particular interest comprises those 1,2-

7-0CH3, 8-0CH3 7-SCH3, 8-0CH3 7-SCH3, 8-SCH3 6-0CH3, 7-0CH3, 8-0CH3

9-NHC(O)C5H<sub>11</sub> 9-NHC(O)CH<sub>2</sub>Br 9-NH-C(NH)NH<sub>2</sub> 9-(2)-thiopbene

benzothiazepines wherein the R1, R2, R3 R4 and R3 radicals are as set forth in

Table 3 below; Re is hydrogen; the R" radical is selected from the group

consisting of hydrogen, methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl and

group of R\* radicals disclosed in Table 2 above. In one embodiment of the benzyl; and the R\* radical or radicals are independently selected from the

compounds of Table 3, for example, q is 1 and  $R^\chi$  is 7-dimethylamino.

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(R<sup>x</sup>)q

R<sup>3</sup>/R

 $R^{1}/R^{2}$ 

9-SCH<sub>2</sub>CH<sub>3</sub> 9-NH<sub>2</sub> 9-NHOH

9-(N)-pyrrolidine 9-(N)-N-methyl-pyrrolidinium, I' 9-(N)-

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211 R5/R6

Compound Number	R¹	R²	R³	R4	R <sup>3</sup>
1452	ethyl	n-butyl	ОН	н	ОН
1453	n-butyl	ethyl	ОН	н	ОН
1454	n-butyl	n-butyl	ОН	н	ОН

1455	ethyl	n-butyl	ОН	Н	NH CO₂H	
1456	n-butyl	ethyl	ОН	н	NH CO <sub>2</sub> H	214
1457	n-butyl	n-butyl	ОН	н	NH CO,H	7

	EHNEOS O					
216		н	но	lyind-a	JAmq-u	1463
	EHNEOS					
		н	но	- स्यंग्रे	n-parkl	79+1
	c HN <sub>5</sub> OS					
		н	но	l⁄tinq-a	сгуλј	1901

	н <sub>5</sub> 03			}		
315	X	н	но	a-butyl	n-prityl	1490
	н+гоэ О					
	×	н	но	cipyl	lyjud-a	1426
	н <sup>€</sup> 03 ✓ ООО					-
i						
		н	но	e-patyl	eqtiλj	0501
		"	HO	fvtsef-r	lvitis	1458

1464	ethyl	n-butyl	ОН	Н	0= Me 0   N   N   N   N   N   N   N   N   N	
1465	n-butyl	ethyl	ОН	Н	0 0-g-Me	2/2
1466	n-butyi	n-butyl	ОН	н	0   0   0   0   0   0   0   0   0   0	

1467	ethyl	n-butyl	ОН	н	0-15
1468	n-butyl	ethyl	ОН	н	
1469	n-butyl	n-butyl	ОН	Н	

			н	но	, ivind-a	ĮÆįnq-u	5241
220			н	но		j.Kinq-a	<b>\$</b> 2 <b>\$</b> 1
		\-\-\-\-\-\-\-\-\-\-\-\-\-\-\-\-\-\-\-	н	но	" "Kinq <b>-u</b>	ефЛ	ELÞI

		Н	но	lçind-a	l⁄zud-a	
319	0 — 0 — 0 M	н	но	ефλј	Įšiną-u	1441
	. o — \$ — • M	н	но	, king-u	сгрλן	0471

1476	ethyl	n-butyl	ОН	Н	No-13-0-	
1477	n-butyl	ethyl	ОН	Н	Mo-15-0.	9.
1478	n-butyl	n-butyl	ОН	н	Me-s-o-	

1479	ethyl	n-butyl	ОН	н	+
					Me—"S—o
					N. N.
1480	n-butyi	ethyl	ОН	н	но
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223		н	но	α-ρπέλη	сџλן	7851
	OH	н	но	JÁ2nq-u	Įćinq-u	1841

1486	n-butyl	ethyl	ОН	н	СО <sub>2</sub> Н	
1487	n-butyl	n-butyl	ОН	Н	СО <sub>2</sub> Н	225

1488	ethyl	n-butyl	ОН	н		
1489	n-butyl	ethyl	ОН	н		7.40
1490	n-butyl	n-butyl	ОН	н	N N	

	HN O	Н	но	lytud-a	сгрλј	<b>1</b> 691
328	O NELS	н	но	a-butyl	а-рацуј	1469
8	E 1 3 N O	н	но	. саруј	l⁄zinq-a	\$661
	O NELS	н	но		сџλј	1464

227	H <sub>2</sub> O3 M	н	но	n-pathl	· ĮÁiną-u	£6 <b>7</b> 1
	H <sub>2</sub> CO <sub>2</sub> H	н	но	сџλן	u-pniλj	1465
	H200, H	Н	но	[Ænq-a	еџλј	16 <b>9</b> 1

1498	n-butyI	ethyl	ОН	н	N NH	
1499	n-butyl	n-butyl	ОН	н	NH NH	
1500	ethyl	n-butyl	ОН	н	2C1	

1501	n-butyl	ethyl	ОН	H	2C1 N* N*
1502	n-butyl	n-butyl	OH	Н	2C1 - N+ N+ N+
1503	ethyl ·	n-butyl	ОН	н	3C1

	M <sub>E</sub> 03					
		н	но	lĄtną-u	ефλј	. 6051
232		н	но	peivi	p.p.ni.j.j	8051
	N H					2.53.
Ĺ	*	н	но	cqti\l	J/Janq-u	۷۵۶۱

					_	
		н	но	iVind-a	сџуλј	9051
231		н	НО	п-рапд	p/sprc/-u	5051
	HO <sub>10</sub> , HO 10 10 10 10 10 10 10 10 10 10 10 10 10	н	но	<b>с</b> фуј	a-butyl	<b>†051</b>

1510	n-butyl	ethyl	ОН	н	о со <sub>2</sub> н	
1511	n-butyl	n-butyl	ОН	н	O CO <sub>2</sub> H	233
1512	ethyl	n-butyl	ОН	н	NH NH 2	

1513	n-butyl	ethyl	ОН	н	*	
					H NH <sub>2</sub>	
					NH	
1514	n-butyl	n-butyl	ОН	н		
					O H NH <sub>2</sub>	234
1515	ethyl	n-butyl	ОН	Н	со з н	
					O NH	
1516	n-butyl	ethyl	ОН	н		
					NH NH	

		H	но	a-butyl	ctbyl	1224
236	-N					
7	<del>*</del>	н	но	n-butyl	n-butyl	5251
	· N · O					
	<del> </del>	н	но	n-pntyl	1/stud-a	1522
	- N					
	• 1	н	но	n-butyl	ефλј	1251

	н со₃н					
		н	но	lyind-n	lyjud-n	0251
	ч <sup>2</sup> оо — О					
235						
23	. 1	н	HO	сфуј	lýtud-a	6151
	H <sub>2</sub> 03—					·
	*	н	но	n-butyl	сгрλј	8151
	ни					
	HE007					
		Н	но	a-butyl	n-butyl	LISI

1525	n-butyl	etby <b>l</b>	ОН	н		
1526	n-butyl	n-butyl	ОН	Н	C1 N: N	
1527	ethyl	n-butyl	ОН	Н	N CO 2 H	437
1528	n-butyl	ethyl	ОН	н	CO <sub>2</sub> H N CO <sub>2</sub> H	

1529	n-butyl	n-butyl	ОН	н.	Со <sup>2</sup> н	
1530	ethyl	n-butyi	ОН	н	O CF <sub>3</sub>	
1531	n-butyl	ethyl	ОН	н	O CF3	38 
1532	n-butyl	n-butyl	ОН	н	O CF.	

	о — — со <sup>3</sup> н					
	<b></b>	н	но	εφλη	p-pntkl	1240
240	H <sup>2</sup> O2—N—N—O					
7	<u> </u>	н	НО	a-butyl	сфуј	1239
	M CO 3 M	н	но	l⁄zud-a	n-butyl	8551
	CO2 N	н	но	edzyl	į Linq-u	LESI

	NE CO NE	н	но	a-pnikj	ефуј	9881
	**************************************	н	но	lyżud-a	l⁄tinq-a	scsi
239	, ch, ch, ch, ch, ch, ch, ch, ch, ch, ch	н	но	cıpλı	į kiną-a	ÞESI
	о — — — — — — — — — — — — — — — — — — —	н	но	l⁄inq-a	сџλј	हरहर

1541	n-butyl	n-butyl	ОН	Н	+	7
					О СО2Н	
1542	ethyl	n-butyl	ОН	н		
					СО2Н	341
1543	n-buty)	ethyl	ОН	н	çо,н	
1544	n-butyl	n-butyl	ОН	н	о созн	_
•					CO <sub>2</sub> H	

1545	ethyl	n-butyl	ОН	н	R = PEG 1000	
1546	n-butyl	ethyl	ОН	н	R = PEG 1000	
1547	a-butyl	n-butyl	ОН	н	R = PEG 1000	747
1548	ethyl	n-butyl	ОН	н	الله الله الله الله الله الله الله الله	

	н	но	ctbyl	lYinq-a	8551
	н	но	l&nq-a	сгрλן	LSSI
244	н	но	a-panikj	a-butyl	9551
	н	но	сџуλן	п-риіді	ssst
ľ	н	но	p-pnràl	сдуλј	<del>)</del> 5551

		н	но	l-find-n	lyind-n	ESSI
		н	но	esph].	JÁ‡nq-u	7551
243		н	но	ĮĄinq−ii	ефλј	1551
		н	70	o-patkj	n-pntλj	occi
	13~~~~~	н	но	lviud-a	[Attic]-u	0551
		н	но	ετρλί	ը-բողչյ	1249

1559	n-butyi	n-butyl	ОН	Н	
1560	ethyl	n-butyl	ОН	н	
1561	n-butyl	n-butyl	ОН	н	
1562	n-butyl	n-buty!	OH	Н	

1563	ethyl	n-butyl	ОН	н	 1
1564	n-butyl	n-butyl	ОН	Н	
1565	n-butyl	n-butyl	ОН	н	246
1566	ethyl	n-butyl	ОН	Н	

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		н	но	n-butyl	εφλι	STZI
	*HN J J					
		н	но	p-pntyl	n-butyl	<b>7</b> L\$1
348	EHN H					
ı		н	но	сфуј	n-pntyl	ELSI
	THN J					
	<b>₹</b>	н	но	u-pntyl	cqr\l	STZI
	нгоз ✓ № Д					
		н	но	n-butyl	1-butyl	1721

	H <sub>2</sub> 03 \ H	Н	но	сџуј	rying-a	OTEI
247	H <sub>E</sub> OO COO JH	н	но	ı∕ınq-a	сџλј	6951
2	.13		-			
						·
		н	но	lywd-a	l/tinq-a	8951
	<u></u>	н	но	c(p)	n-pntλ <u>ı</u>	<i>1</i> 951

1576	n-butyl	ethyl	ОН	Н	
1577	n-butyl	n-butyl	ОН	н	
1578	ethyl	n-butyl	ОН	Н	244
1579	a-butyl	ethyl	ОН	н	

1580	n-butyl	n-butyl	ОН	н		1
1581	ethyl	n-butyl	ОН	Н	<u></u>	1
					Ryo ci	
					X X X	
1582	n-butyl	ethyl	ОН	Н	<u></u>	250
					( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( )	6
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1583	n-butyl	n-butyl	ОН	н	<u></u>	1
					(	
					N N N N N N N N N N N N N N N N N N N	

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	H <sub>z</sub> OO <sub>2</sub> H					
	Н Н	но	n-butyl	ефλј	<i>L</i> 851	تو
7	H CD <sup>2</sup> H					
257	Д	но	a-butyl	lytud-a	9851	
	H CO <sup>2</sup> H					
	н	но	сару	n-butyl	1282	
	H CO <sup>3</sup> H					
	н	но	n-butyl	eqrix	<b>≯8</b> 51	

	H <sub>E</sub> O <sub>2</sub> H					
		н	но	еділі	lytud-a	1651
-6	H <sup>C</sup> CO <sup>2</sup> H	н	но	p-pnt/st	espyl	0651
252	и <sup>с</sup> оэ и со <sup>3</sup> н	н	но	į kiną-a	į (Amq-a	. 6851
	н <sub>2</sub> 00 м					
	<del></del>	н	но	егр\л	iyind-a	8881

1592	n-butyl	n-butyi	ОН	н	СО <sub>2</sub> Н
1593	ethyl	n-butyl	ОН	н	N N N N N N N N N N N N N N N N N N N
1594	n-butyl	n-butyl	ОН	н	
1595	n-butyl	n-buty!	ОН	н	

1596	ethyl	n-butyl	ОН	н		١
					CO <sub>2</sub> H	
1597	n-butyl	etbyl	ОН	н .		
1598	n-butyl	n-butyi	ОН	н	CO <sub>2</sub> H	354
1599	ethyl	n-butyl	ОН	н	CH <sub>3</sub>	

	H*OS ~ N N N N N N N N N N N N N N N N N N					
	大	н	но	a-butyl	a-butyl	<i>L</i> 091
	H <sub>2</sub> OS ~ M H H H					
256	<del>\_</del> '	н	но	егрλј	a-butyl	9091
	H <sup>c</sup> os ~ M H					
ľ	7	н	но	a-butyl	ετρλι	\$091
	io , io , io , io , io , io , io , io ,					
	7	н	но	1\frac{1}{2}	ր/չող-ա	1604

	CH3 CH3					
	*	н	но	epply	n-path]	. £091
255	е с с с с с с с с с с с с с с с с с с с					
Ï	<del> </del>	H	но	n-pntyl	сгуλј	1602
	CI.	н	но	lyind-a	lyind-n	1091
	C1.	н	но	ефλ	ը-թուծլ	0091

1608	ethyl	n-butyl	ОН	н	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
1609	n-butyl	ethyl	ОН	Н	N CO <sub>2</sub> H H CH <sub>3</sub>	
1610	n-butyi	n-butyl	OH	н	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	357
1611	ethyl	n-butyl	он	н	O O SO, H	<b>T</b>

1612	n-butyl	ethyl	ОН	н	₹,°° ,° so,н	-
1613	n-butyl	n-butyl	ОН	н	о о о о о о о о о о о о о о о о о о о	
1614	ethyl	a-butyl	ОН	H	n=0 or a positive integer	358
1615	a-butyl	ethyl	ОН	н	n=0 or a positive integer	

	HO HO HO N N N N N N N N N N N N N N N N	н	но	<b>у</b> сцэ	<b>յ</b> Հ <b>Լ</b> ոգ-ս	
360	HO HO O HO N H	н	но	l/stud-n	łyńte	1620
	HO HO HO H	н	но	k/sjnq-u	μ <b>ζ</b> şnq-u	6191

	HO HO HO H	н	но	үйдө	l/ţnq-u	8181
259	HO HO HO H	н	но	րչուժ-ը	сфλј	<b>L</b> 191
	**************************************	н	но	Iężind-ri	Į.∕anq-α	9191

1622	n-butyl	n-butyl	ОН	Ħ	OH OH OH
1623	ethyl	n-butyl	ОН	н	он он он
1624	n-butyl	ethyl	ОН	H	он он он он

1625	n-butyl	n-butyl	ОН	н	OH OH
1626	ethyl	n-butyl	ОН	н	HO HO HO HO HO HO HO HO HO HO HO HO HO H
1627	n-butyl	ethyl	ОН	н	OR OR OR OR OR OR OR OR OR OR OR OR OR O

+	HO OH H	н	но	сфЛј	king-a	CE91
764	HO HO HO HI HI HI HI HI HI HI HI HI HI HI HI HI					
	HO OH H	н	но	l/Jud-a	сцАј	1632
L		H	но	n-butyl	n-butyl	1631

	HO OH H N	н	но	сфАј	Iężną-a	0691
265	HO OH H N	н	но	Jánq-u	crpλj	6291
	HO HO HO HO HO HO HO HO HO HO HO HO HO H	н	но	rywy-a	jkinq-u	1938

1634	n-butyl	n-butyl	ОН	н	но он он
1635	ethyl	n-buty!	ОН	н	но он он
1636	n-butyl	ethyl	ОН	н	но он он он он

						·
-	1637	n-butyl	n-butyl	ОН	н	но он он
	1638	ethyl	n-butyl	ОН	H	он он он
	1639	n-butyl	ethyl	ОН	н	он он он

	HO OH					
I		H	но	сфуј	a-butyl	S#91
398	HO OH II	н	но	Jáznq-u	ефλן	1191
	HO HO H	н	но	į kiną-u	iViud-a	1943

	HO HO HO HI	н	но	ефλן	a-buryl	1642
247	HO HO HI HI HI HI HI HI HI HI HI HI HI HI HI	н	но	rpanyl	сџλј	1191
	но он во он	н	но	n-buryl	n-patyl	0191

1646	n-butyl	n-butyl	ОН	н	HE COH COH
1647	ethyl	n-butyl	OH	н	но он
1648	n-butyl	ethyl .	ОН	н	он он

1649	n-butyl	n-butyl	OH	Н	но он он
1650	ethyl	n-butyl	ОН	н	HO OH OH
1651	n-butyl	ethyl	ОН	н	и но он он

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Another group of compounds of interest consists of those compounds of Formula I wherein  $\,R^{1}$  and  $R^{2}$  are alkyl, preferably n-butyl; \,\,R^{3} is hydroxy; group consisting of amino, dimethylamino and methoxy; and R3 is phenyl R' and R' are hydrogen; R' is hydrogen; R' radicals are selected from the substituted at the para or meta position with one of the following groups:

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O R = 1000 MW PEG

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Mn", Fe", Fe", Ni", Ni", Cr", Cu", Za", Cd", Ga", In", V", Ru", Pt", Rh" wherein M is selected from the group consisting of Con, Com, Mnn, and Iru.

## Dosages. Formulations, and Routes of Administration

hyperlipidemic diseases, conditions and/or disorders by any means, preferably oral, that contacts these compounds with their site of action in the body, for The iteal bile acid transport inhibitor compounds of the present invention can be administered for the prophylaxis and/or treatment of example in the ileum of a mammal such as a human.

2

For the prophylaxis and/or treatment of the diseases, conditions and/or disorders referred to above, the compounds of the present invention can be used as the compound per se. Pharmaceutically acceptable salts are

particularly suitable for medical applications because of their greater aqueous pharmaceutically acceptable anion or cation. Suitable pharmaceutically solubility relative to the parent compound. Such salts comprise a 15

potassium salts, and alkaline earth salts such as magnesium and calcium salts. appropriate include ammonium salts, alkali metal salts such as sodium and medical purposes. Suitable pharmaceutically acceptable base saits where and trifluoroacetic acids. The chloride salt is particularly preferred for citric, ethanesulfonic, fumaric, gluconic, glycolic, isothionic, lactic, hydrochloric, hydrobromic, phosphoric, metaphosphoric, nitric, sulfonic, and lactobionic, maleic, malic, methanesulfonic, succinic, toluenesulfonic, tartaric, sulfuric acids, and organic acids such as acetic, benzenesulfonic, benzoic, appropriate include those salts derived from inorganic acids, such as acceptable acid addition salts of the compounds of the present invention where

pharmaceutically acceptable anions such as those anions selected, for example, The anions of the definition of A' in the present invention are 5

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by any of the well known techniques of pharmacy, consisting essentially of or both, and is preferably formulated with the compound as a unit-dose the form of a pharmaceutical composition comprising additional ingredients admixing the components invention. The pharmaceutical compositions of the invention can be prepared substances can also be present, including other compounds of the present to 95% by weight of the active compound. Other pharmacologically active composition, for example, a tablet or capsule, which can contain from 0.05% not deleterious to the recipient. A carrier material can be a solid or a liquid, materials are compatible with the other ingredients of the composition and are (collectively referred to herein as "carrier materials"). Acceptable carrier such as acceptable carriers, diluents, excipients, adjuvants and the like The compounds of the present invention also can be administered in

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available for use in conjunction with pharmaceuticals, either as an individual therapeutic compound in a monotherapeutic regimen or as a combination of These compounds can be administered by any conventional means ß

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therapeutic compounds in a combination therapy regimen

administration, and the clinical condition of the recipient biological effect will depend on a number of factors such as the specific compound chosen, the use for which it is intended, the mode of The amount of compound that is required to achieve the desired

single dose, or in proportionate multiple subdoses. Subdoses can be bodyweight/day. This total daily dose can be administered to the patient in a administered 2 to 6 times per day. Doses can be in sustained release form bodyweight/day, and more preferably from about 3 to about 10 mg/kg effective to obtain desired results. 100 mg/kg bodyweight/day, preferably from about 1 mg to about 50 mg/kg In general, a daily dose can be in the range of from about 0.3 to about

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15 more preferably from about 10 to about 50 mg of compound. In the case of benzothiazepine compound, preferably about 1 to about 75 mg of compound pharmaceutically acceptable salts, the weights indicated above refer to the capsules, can contain, for example, from about 0.1 to about 100 mg of weight of the benzothiazepine ion derived from the salt. Orally administrable unit dose formulations, such as tablets or

23 20 mucosal lining of the intestinal tract, or enzymatic release of the active drug physical properties of the formulation, bioadhesion of the dosage form to the number of mechanisms. These include, but are not limited to, pH sensitive prolonged or sustained delivery of the drug to the gastrointestinal tract by any invention can include formulations, as are well known in the art, to provide manipulation of the dosage form. Thus, enteric-coated and enteric-coated which the active drug molecule is delivered to the site of action (the ileum) by from the dosage form. The intended effect is to extend the time period over release from the dosage form based on the changing pH of the small intestine slow erosion of a tablet or capsule, retention in the stomach based on the Oral delivery of an ileal bile acid transport inhibitor of the present

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controlled release formulations are within the scope of the present invention. Suitable enteric coatings include cellulose acetate phthalate, polyvinylacetate phthalate, hydroxypropylmethylcellulose phthalate and anionic polymers of methacrylic acid and methacrylic acid methyl ester.

When administered intravenously, the dose can, for example, be in the range of from about 0.1 mg/kg body weight to about 1.0 mg/kg body weight, preferably from about 0.25 mg/kg body weight, and more preferably from about 0.4 mg/kg body weight, and more preferably from about 0.4 mg/kg body weight to about 0.6 mg/kg body weight. This dose can be conveniently administered as an

infusion of from about 10 ng/kg body weight to about 100 ng/kg body weight per minute. Infusion fluids suitable for this purpose can contain, for example, from about 0.1 ng to about 10 mg, and preferably from about 1 mg to about 10 mg per milliliter. Unit doses can contain, for example, from about 1 mg to about 10 g of the compound of the present invention. Thus, ampoules for injection can contain, for example, from about 1 mg to about 100 mg.

Pharmaceutical compositions according to the present invention include those suitable for oral, rectal, topical, buccal (e.g., sublingual), and parenteral (e.g., subcutaneous, intramuscular, intradermal, or intravenous) administration, although the most suitable route in any given case will depend on the nature and severity of the condition being treated and on the nature of the particular compound which is being used. In most cases, the preferred route of administration is oral.

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Pharmaceutical compositions suitable for oral administration can be presented in discrete units, such as capsules, cachets, lozenges, or tablets, each containing a predetermined amount of at least one compound of the present invention; as a powder or granules; as a solution or a suspension in an aqueous or non-aqueous liquid; or as an oil-in-water or water-in-oil emulsion. As indicated, such compositions can be prepared by any suitable method of pharmacy which includes the step of bringing into association the active

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compound(s) and the carrier material (which can constitute one or more accessory ingredients). In general, the compositions are prepared by uniformly and intimately admixing the active compound with a liquid or finely divided solid carrier material, or both, and then, if necessary, shaping the

- product. For example, a tablet can be prepared by compressing or molding a powder or granules of the compound, optionally with one or more assessory ingredients. Compressed tablets can be prepared by compressing, in a suitable machine, the compound in a free-flowing form, such as a powder or granules optionally mixed with a binder, lubricant, inert diluent and/or surface
  - 10 active/dispersing agent(s). Molded tablets can be made by molding, in a suitable machine, the powdered compound moistened with an inert liquid diluent.

Pharmaccutical compositions suitable for buccal (sub-lingual) administration include lozenges comprising a compound of the present invention in a flavored base, usually sucrose, and acacia or tragacanth, and pastilles comprising the compound in an inert base such as gelatin and glycerin or sucrose and acacia.

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Pharmaceutical compositions suitable for parenteral administration conveniently comprise sterile aqueous preparations of a compound of the present invention. These preparations are preferably administered intravenously, although administration can also be effected by means of subcutaneous, intramuscular, or intradermal injection. Such preparations can conveniently be prepared by admixing the compound with water and rendering the resulting solution sterile and isotonic with the blood. Injectable

compositions according to the invention will generally contain from 0.1 to 5% w/w of a compound disclosed herein.

Pharmaceutical compositions suitable for rectal administration are preferably presented as unit-dose suppositories. These can be prepared by admixing a compound of the present invention with one or more conventional

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resulting mixture. solid carrier materials, for example, cocoa butter, and then shaping the

aerosol, or oil. Carrier materials that can be used include vaseline, lanoline, polyethylene glycols, alcohols, and combinations of two or more thereof. The w/w of the composition, for example, from 0.5 to 2%. active compound is generally present at a concentration of from 0.1 to 15% skin preferably take the form of an ointment, cream, lotion, paste, gel, spray, Pharmaceutical compositions suitable for topical application to the

5 A suitable concentration of the active compound is about 1% to 35%, as described in Pharmaceutical Research, 3(6), 318 (1986). be delivered from the patch by electrotransport or iontophoresis, for example, preferably about 3% to 15%. As one particular possibility, the compound can compositions suitable for transdermal administration can be presented as the recipient for a prolonged period of time. Such patches suitably contain a solution, dissolved and/or dispersed in an adhesive, or dispersed in a polymer. compound of the present invention in an optionally buffered, aqueous discrete patches adapted to remain in intimate contact with the epidermis of Transdermal administration is also possible. Pharmaceutical

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20 vary depending upon the host treated and the particular mode of the carrier materials to produce a single dosage form to be administered will In any case, the amount of active ingredient that can be combined with

in normal practice, additional substances other than inert diluents, e.g., such as sucrose, lactose, or starch. Such dosage forms may also comprise, as compounds of the present invention admixed with at least one inert diluent tablets, pills, powders, and granules noted above comprise one or more and pills, the dosage forms may also comprise buffering agents. Tablets and lubricating agents such as magnesium stearate. In the case of capsules, tablets The solid dosage forms for oral administration including capsules,

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pills can additionally be prepared with enteric coatings

compositions may also comprise adjuvants, such as wetting agents elixirs containing inert diluents commonly used in the art, such as water. Such pharmaceutically acceptable emulsions, solutions, suspensions, syrups, and emulsifying and suspending agents, and sweetening, flavoring, and perfuming Liquid dosage forms for oral administration can include

ដ 5 solution. In addition, sterile, fixed oils are conventionally employed as a suitable dispersing or setting agents and suspending agents. The sterile such as oleic acid find use in the preparation of injectables. employed including synthetic mono- or diglycerides. In addition, fatty acids solvent or suspending medium. For this purpose any bland fixed oil may be may be employed are water, Ringer's solution, and isotonic sodium chloride a nontoxic parenterally acceptable diluent or solvent, for example, as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that injectable preparation may also be a sterile injectable solution or suspension in oleaginous suspensions may be formulated according to the known art using Injectable preparations, for example, sterile injectable aqueous or

foregoing and the like. Pharmaceutically acceptable carrier materials encompass all the

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## Treatment Regimen

23 blood levels with the compounds and/or compositions of the present invention disease, the route of administration, pharmacological considerations such as weight, sex, diet, and medical condition of the patient, the severity of the is selected in accordance with a variety of factors. These include the type, age, disease, condition and/or disorder relating to hyperlipemia, e.g., atherosclerosis, or to protect against or treat further high cholesterol plasma or The dosage regimen to prevent, give relief from, or ameliorate a

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the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized, and whether the compound is administered as part of a drug combination. Thus, the dosage regimen actually employed may vary widely and therefore

Initial treatment of a patient suffering from a hyperlipidemic condition can begin with the dosages indicated above. Treatment should generally be continued as necessary over a period of several weeks to several months or years until the hyperlipidemic disease condition has been controlled or

deviate from the preferred dosage regimen set forth above.

eliminated. Patients undergoing treatment with the compounds or compositions disclosed herein can be routinely monitored by, for example, measuring serum cholesterol levels by any of the methods well known in the art, to determine the effectiveness of therapy. Continuous analysis of such data permits modification of the treatment regimen during therapy so that optimal effective amounts of compounds of the present invention are administered at any point in time, and so that the duration of treatment can be determined as well. In this way, the treatment regimen/dosing schedule can be rationally modified over the course of therapy so that the lowest amount of iteal bile acid transport inhibitor of the present invention which exhibits satisfactory effectiveness is administered, and so that administration is continued only so long as is necessary to successfully treat the hyperlipidemic condition.

The following non-limiting examples serve to illustrate various aspects of the present invention.

## Examples of Synthetic Procedures

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The starting materials used in the preparation of the compounds of the following examples, as well as other compounds of the present invention, are commercially available or can be prepared by conventional methods known to one of ordinary skill in the art or in an analogous manner to conventional

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methods described in the art. The starting materials of the following examples were obtained from commercial sources unless otherwise noted. The ethyl 2-amino-2-butylhexanoate hydrochloride used below was prepared in an analogous manner to the literature method of Stork (J. Org. Chem. 41, 349)

Example 1

(1976).

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

Step 1. 2-Amino-2-butylhexanol

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To a solution of 29.75 g (0.12 mol) of ethyl 2-amino-2-butylhexanoate hydrochloride in 100 mL of tetrahydrofuran cooled to -20 °C was added 148.8 mL of a 1.0 M solution of lithium aluminum hydride in tetrahydrofuran while

- ö tetrahydrofuran and concentrated to give 20.61 g of 2-amino-2-butylhexanol sulfate and concentrated. The resulting yellow oil was dissolved in 300 mL of acetate. The ethyl acetate solution was washed with water (2x200 mL) and then brine (300 mL). The ethyl acetate layer was dried over magnesium temperature. The resulting slurry was filtered and washed with 100 mL ethyl The reaction mixture was stirred for one hour and warmed to room

Step 2. N-[1-Butyl-1-(hydroxymethyl)pentyl]-4-fluorobenzenesulfonamide

chloride in 150 mL of tetrahydrofuran was added 36.4 mL of triethylamine. To a solution of 16.95 g (0.09 mol) of 4-fluorobenzene sulfonyl

2 [1-butyl-1-(hydroxymethyl)pentyl]-4-fluorobenzenesulfonamide as an oil. was washed with water (2  $\times$  200 mL) and brine (300 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated to give 29.47 g of Nat room temperature. The reaction mixture was concentrated and then the added. The reaction mixture was stirred 30 minutes at 0 °C and then 16 hours 2-butylhexanol (prepared in step 1 above) in 70 mL of tetrahydrofuran was The reaction mixture was cooled to 0 °C and a solution of 19.61 g of 2-aminoresidue was dissolved in 250 mL of ethyl acetate. This ethyl acetate solution

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Step 3. N-(1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino) benzenesulfonamide

as an solid. dimethylamine was prepared and placed in a bomb. The reaction mixture was N-[1-butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)benzenesulfonamide heated to 110 °C for 16 hours, cooled, and then concentrated to give 25.46 g of above, 872 mL of 2.0 M dimethylamine in tetrahydrofuran and 100 mL of neat A solution containing 28.89 g (0.09 mol) of the oil prepared in Step 2

5 4-(dimethylamino)benzenesulfonamide Step 4. N-[1-Butyl-1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-

The ethyl acetate solution was washed with 5% hydrochloric acid solution (2 x prepared in Step 3 and then 14.01 g of imidazole. The reaction mixture was stirred 3 days and then diluted with 1 L of ethyl acetate and 500 mL of water. 158 mL of dimethylformamide was added 24.46 g (0.07 mol) of the solid To a solution of 15.51 g (0.10 mol) of t-butyldimethylsilyl chloride in

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stirred with hexane and the resulting solid was filtered to give 25.31 g of  $\mathcal{N}$ -{1-200 mL), water (200 mL) and then brine (200 mL). The ethyl acetate layer was dried with magnesium sulfate and concentrated to an oil. The oil was butyl-1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]4-(dimethylamino)benzenesulfonamide as a white solid.

Step 5. N-[1-Butyl-1-[[[(1,1dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-N-methylbenzenesulfonamide

dispersion in mineral oil in 43 mL of tetrahydrofuran was added 4.0 g (8.50 To a solution of 0.476 g (11.90 mmol) of 60% sodium hydride

- concentrated and 250 mL ethyl acetate and 250 mL water added. The layers sulfate dropwise. The reaction mixture was heated at reflux for one hour, mmol) of the solid prepared in Step 4 above and then 1.6 mL of dimethyl cooled to 0 °C, and then water was added. The reaction mixture was were separated and the ethyl acetate solution was washed with 1 M 2
- hydrochloric acid (2 x 200 mL), saturated sodium bicarbonate (2 x 200 mL), residue was purified by flash chromatography with 15% ethyl acetate/hexane as cluent to give 3.35 g of N-[1-butyl-1-[[[(1,1dimethylethyl) dimethylsilyl] water (200 mL) and then brine (200 mL). The ethyl acetate layer was dried oxy]methyl]pentyl]-4-(dimethylamino)-N-methylbenzenesulfonamide as an over magnesium sulfate and concentrated to give 4.63 g of a residue. The 2 2

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Step 6.

To a solution of 3.35 g (6.90 mmol) of the oil prepared in Step 5 above 1.6 M n-butyllithium in hexanes. The reaction mixture was stirred 30 minutes in 35 mL of tetrahydrofuran cooled to 0 °C was added dropwise 9.66 mL of at 0 °C, warmed to room temperature, and stirred one hour. To the reaction magnesium sulfate and concentrated to give 3.12 g of a yellow solid. Tetrahydrofuran was evaporated. To the residue was added 200 mL dichloromethane layer was washed with brine (200 mL), dried over dichloromethane and 200 mL water and the layers separated. The mixture was added 6.5 mL of 5% hydrochloric acid and then the 2

Step 7. N-[1-Butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide

To a solution of 130 mg (0.11 mmol) of tetrakis(triphenylphosphine) palladium(0) in 10 mL of toluene was added 825 mg of 3-nitrobenzyl

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bromide. After the tohucne solution was stirred 10 minutes, a degassed solution of 2.02 g (3.82 mmol) of the solid prepared in Step 6 above in 8 mL ethanol was added followed by 10 mL of 1 M sodium carbonate. The reaction mixture was heated at reflux 45 minutes and then cooled and concentrated. To the residue was added 250 mL of ethyl acetate. The ethyl acetate mixture was

- the residue was added 250 mL of ethyl acetate. The ethyl acetate mixture was washed with brine (2 x 200 mL), dried over magnesium sulfate and concentrated to give 2.76 g of a residue. To the residue was added 200 mL of 30% ethyl acetate in hexane, and the mixture was stirred 1.5 hours and then filtered through silica. The ethyl acetate solution was concentrated to give
- 2.30 g of N-[1-bütyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide as a yellow solid.

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Step 8. N-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-{(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide

above in 10 mL of tetrahydrofuran cooled to 0 °C was added 4.4 mL of 1 M tetrahutylammonium fluoride in tetrahydrofuran. The reaction mixture was stirred 15 minutes at 0 °C and then 12 hours at room temperature. To the reaction mixture was added 250 mL of ethyl acetate. The ethyl acetate solution was washed with water (200 mL) and brine (200 mL). The ethyl

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acetate layer was dried over magnesium sulfate and concentrated to give 1.88 g of a brown oil residue. The residue was purified by flash chromatography with 30% ethyl acetate in hexane as eluent to give 1.49 g of N-[1-butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide as a yellow oil.

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Step 9. N-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl) methyl]-N-methylbenzenesulfonamide.

To a solution of 1.49 g (2.95 mmol) of the oil prepared in Step 8 above in 10 mL of dimethylsulfoxide was added 1.23 mL of triethylamine and then 1.41 g of sulfur trioxide pyridine complex. The reaction mixture was stirred one hour and then diluted with 200 mL water. The aqueous mixture was washed with ethyl acetate (3 x 100 mL). The combined organic layers were washed with 5% hydrochloric acid (100 mL) and brine (100 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated. The residue was purified by flash chromatography with 25% ethyl acetate in hexane as eluent to give 1.31 g of N-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)]-M-methylbenzenesulfonamide as a yellow oil.

Step 10. (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

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To a solution of 504 mg (2.60 mmol) of the oil prepared in Step 9 above in 50 mL of tetrahydrofuran cooled to 0 °C was added 2.80 mL of 1 M potassium t-butoxide in tetrahydrofuran. The reaction mixture was stirred for 15 minutes, water was added, and then the mixture was concentrated to yield a residue. The residue was dissolved in 100 mL ethyl acetate. The ethyl acetate solution was washed with water (100 mL) and brine (100 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated to give 1.25 g of a semi-solid. The residue was purified by crystallization with ethyl acetate and hexane to give 737.5 mg of (4K,5R)-3,3-dibutyl-7.

(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide as a yellow crystalline solid. <sup>1</sup>H NMR (CDCl<sub>1</sub>) 6 0.90-1.00 (m, 6H), 1.05-1.80 (m, 12H), 2.50-2.60 (m, 1H), 2.79 (s, 6H), 2.85 (s, 3H), 4.09 (d, J=9.0 Hz, 1H), 5.76 (d, J=2.0 Hz, 1H), 5.88 (s, 1H), 6.53 (dd, J=2.4, 8.9 Hz, 1H), 7.59 (t, J=7.9 Hz, 1H), 7.84-7.88 (m, 2H), 8.22 (dd, J=1.0, 8.1 Hz, 1H), 8.47 (s, 1H). MS (M+H') 504.

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### Example 2

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(4R,5R)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide

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A solution of 737 mg (1.46 mmol) of the solid prepared in Step 10 of Example 1 was dissolved in 110 mL of ethanol in a 3 oz. Fisher/Porter vessel, and about 150 mg of 10% Pd/C catalyst was added. This mixture was hydrogenated at 40 psi H<sub>2</sub> for 20 hours and then fillered. The filtrate was

5 concentrated to give 0.82 g of a semi-solid material. The semi-solid material was crystallized from ethyl acetate and hexane to give 0.51 g of (4R,5R)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrabydro-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide as colorless crystals. <sup>1</sup>H NMR (CDCl<sub>3</sub>) 6 0.89 (t, J = 6.6 Hz, 3H), 0.92 (t, J = 7.2 Hz, 3H), 1.10-1.45 (m, 8H), 1.60-1.75 (m, 3H), 1.98-2.10 (m, 1H), 2.48-2.58 (m, 1H), 2.79 (s, 6H), 2.81 (s, 3H), 3.69 (s, 2H), 4.12 (d, J = 7.8 Hz, 1H), 5.62 (s, 1H), 6.07 (d, J = 2.1 Hz, 1H), 6.46 (dd, J = 2.4, 8.7 Hz, 1H), 6.61 (br d, J = 7.8 Hz, 1H), 6.80 (br s, 1H), 6.89 (br d, J = 2.1 Hz, 1H), 7.15 (t, J = 7.8 Hz, 1H), 7.79 (d, J = 8.7 Hz, 1H) MS (M+H') 474.

## Example 3

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5-bromo-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazzpin-5-yl]phenyl]pentanamide

To a solution of 0.25 g (0.53 mmol) of the solid prepared in Example 2

mL). The ethyl acetate layer was dried over magnesium sulfate and  $\times$  25 mL), saturated sodium bicarbonate solution (2  $\times$  25 mL) and brine (25 The combined ethyl acetate layers were washed with 5% hydrochloric acid (2 residue. The aqueous solution was extracted with ethyl acetate (2  $\times$  50 mL).

concentrated to give 0.29 g of a solid. The solid was purified by

2 5 4H), 7.76 (br s, 1H), 7.80 (d, J=8.7 Hz, 1H). MS (M+H\*) 636, 638. 1H), 5.69 (s, 1H), 5.97 (s, 1H), 6.47 (dd, J = 2.4, 8.9 Hz, 1H), 7.24-7.40 (m, solid. 'H NMR (CDCl<sub>3</sub>)  $\delta$  0.88 (t, J = 7.2 Hz, 3H), 0.92 (t, J = 6.9 Hz, 3H), methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]pentanamide as a tan [3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2crystallization with ethyl acetate and hexane to give 202.3 mg of 5-bromo-N-1H), 2.78 (s, 6H), 2.81 (m, 3H), 3.41 (t, J = 6.3 Hz, 2H), 4.10 (d, J = 8.5 Hz, 1.20-1.42 (m, 8H), 1.57-2.10 (m, 8H), 2.37 (t, J= 6.9 Hz, 2H), 2.46-2.57 (m,

methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-N,N,N-triethyl-5-5-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-

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oxo-pentanaminium trifluoroacetate

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70 with the product. MS (M') 657: oxo-pentanaminium trifluoroacetate as a white solid. 1H NMR was consistent methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-N,N,N-triethyl-5by reverse phase high pressure liquid chromatography to give 16.2 mg of 5reaction mixture was concentrated to form a residue. The residue was purified mixture was heated at 55 °C for 28 hours and then at 75 °C for 16 hours. The above in 1 mL of acetonitrile was added 87  $\mu$ L of triethylamine. The reaction To a solution of 100 mg (0.16 mmol) of the solid prepared in Example 3 [[3-[(4R,5R)-3,3-dibuty]-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-

2-chloro-N-[3-[(4R,SR)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]acetamide

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To a solution of 100 mg (0.21 mmol) of the solid prepared in Example 4 above in 2 mL of tetrahydrofuran was added 29 mg of bromoacetic acid, 29 µL of triethylamine, and then 40 mg of

- ethyldimethylaminopropylcarbodiimide hydrochloride. The reaction mixture was stirred 16 hours and then 50 mL ethyl acetate was added. The ethyl acetate solution was washed with water, 5% hydrochloric acid (2 x 25 mL), saturated sodium bicarbonate solution (2 x 25 mL), and then brine (25 mL). The ethyl acetate layer was dried over magnesium sulfate and then
- 10 concentrated to give 88 mg of an oil. The oil was purified by flash chromatography with 50% ethyl acetate in hexane as eluent to give 72.0 mg of cir-3,3-dibutyl-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-7-dimethylamino-5-(3-(2-chloroaceamido)phenyl)-1,2-benzothiazepine with a trace of 2-chloro-N-[3-(4R,SR)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-
  - 15 methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]acetamide present. ¹H
    NMR was consistent with the product. MS (M+H\*) 550.

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Example 6

2-[[3-[(4R,SR)-3,3-dibutyl-7-(dimethylamino]-2,3,4,5-tetrabydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-N,N,N-triethyl-2-oxoethanaminium chloride

To a mixture of 63 mg (0.12 mmol) of the material prepared in Example 5 above in 1 mL of tetrahydrofuran was added 64 μL of triethylamine. The reaction mixture was heated to reflux for three days and then concentrated. The residue was triturated with ether to give 66.5 mg of 2[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino]-2,3,4,5-tetrahydro-4-hydroxy-2methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-N,N,V-triethyl-2oxoethanaminium chloride as a tan solid. <sup>1</sup>H NMR was consistent with the product. MS (M\*) 615.

Example 7

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-

15 methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide

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Step 1. N-[1-Butyl-1-[[[(1-dimethylethyl)]dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-N-methylbenzenesulfonamide

To a solution of 1.00 g (2.06 mmol) of the material from Step 5 of Example 1 above in 10 mL of tetrahydrofuran cooled to 0 °C was added 2 mL of 1.6 M n-butyllithium in hexanes. The reaction mixture was stirred one hour at 0 °C. To the reaction mixture was added 480 µL of trimethyl borate and the mixture stirred 15 minutes at 0 °C and then one hour at room temperature. The reaction mixture was concentrated to form a residue. The residue was dissolved in 20 mL of toluene and 2.1 mL of 2 M aqueous sodium carbonate.

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To the mixture was added 300 µL of p-methoxybenzyl chloride and then 71 mg of tetrakis(triphenylphosphine)palladium(0). The reaction mixture was heated at 100 °C for 16 hours, cooled, and then 50 mL of toluene added. The reaction mixture was washed with water (50 mL) and brine (50 mL), filtered through silica, and concentrated to form a residue. The residue was purified by flash chromatography to give 0.82 g of N-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-N-methylbenzenesulfonamide as an oil.

Step 2. N-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(4-10 methoxyphenyl)methyl]-N-methylbenzenesulfonamide

The procedure of Step 8 of Example 1 above was followed except that N-[1-butyl-1-[[[(1-dimethylethyl)dimethylsityl]oxy]methyl]pentyl]-4(dimethylamino)-2-[(4-methoxyphenyl)methyl]-N-methylbenzenesulfonamide was used in place of N-[1-butyl-1-[[[(1-dimethylethyl)dimethylsityl]oxy] methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-

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methylbenzenesulfonamide.

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Step 3. N-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl) methyl]-N-methylbenzenesulfonamide

The procedure of Step 9 of Example 1 above was followed except that N-[1-butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(4-

methoxyphenyl)methyl}-W-methylbenzenesulfonamide was used in place of N-[1-butyl-1-(hydroxymethy))pentyl]-4-(dimethylamino)-2-[(3-nitophenyl)methyl]-W-methylbenzenesulfonamide.

Step 4. (48,58)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide

- 10 The procedure of Step 10 of Example 1 above was followed except that N-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-N-methylbenzenesulfonamide was used in place of N-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide.
- 15 'H NMR (CDCI,) 8 0.83-0.96 (m, 6H), 1.15-1.38 (m, 6H), 1.69-1.83 (m, 4H), 2.00-2.08 (m, 1H), 2.55-2.59 (m, 1H), 2.81 (s, 6H), 2.83 (s, 3H), 3.84 (s, 3H), 4.10-41.6 (m, 1H), 5.70 (s, 1H), 5.99 (s, 1H), 6.52 (s, 1H), 6.93 (d, J= 8.6 Hz,

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2H), 7.43 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 8.6 Hz).

Example 8

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide

To a solution of 0.52 g (1.06 mmol) of the solid prepared in Step 4 of Example 7 above in 10 mL of dichloromethane cooled to -78 °C was added 300 µL of boron tribromide. The reaction mixture was stirred for one hour at

- 10 78 °C and then 100 mL of water and 100 mL of dichloromethane were added.
  The dichloromethane solution was washed with 10% aqueous sodium carbonate(100 mL), 10% hydrochloric acid (100 mL) and brine (100 mL).
  The dichloromethane layer was dried over magnesium sulfate and concentrated to give 0.46 g of (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-1 tetrahydro-5-(4-hydroxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide as a solid. ¹H NMR (CDCl,) 8 0.82-0.97 (m, 6H), 1.15-1.40 (m, 6H), 1.67-1.76 (m, 4H), 2.00-2.10 (m, 1H), 2.51-2.59 (m, 1H), 2.83 (s, 6H), 2.84 (s, 9H), 4.12 (d, J=8.0 Hz, 1H), 4.88 (tr s, 1H), 5.69 (s, 1H), 6.07 (d, J=2.2 Hz, 1H), 6.60 (dd, J=2.2, 8.6 Hz, 1H), 6.88 (d, J=8.6 Hz, 2H), 7.38 (d, J=8.3 Hz,
- 20 2H), 7.85 (d, J = 8.6 Hz). HRMS (ES) Calc'd for C<sub>26</sub>H<sub>39</sub>N<sub>3</sub>O<sub>4</sub>S: 475.2631.

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Found: 475.2649.

iodoethyoxy)ethoxy)ethoxy)phenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-(4R,SR)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-(((2-

iodoethyoxy)ethoxy)ethoxy)phenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1ethyl acetate and the reaction mixture extracted with ethyl acetate. The ethyl dioxide as a solid. HRMS (ES) Calc'd for C<sub>22</sub>H<sub>50</sub>N<sub>2</sub>O<sub>6</sub>SI: 717.2434. Found: of (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-(((2chromatography with 10-25% ethyl acetate in hexane as eluent to give 0.37 g and concentrated to form a residue. The residue was purified by flash acetate layer was washed with brine (100 mL), dried over magnesium sulfate one hour. To the reaction mixture was added 100 mL of water and 100 mL of in 8 mL dimethylformamide was added 44 mg of 95% sodium hydride and then 730 µL of 1,2-bis(2-iodoethoxy)ethane. The reaction mixture was stirred To a solution of 0.38 g (0.80 mmol) of the solid prepared in Example 8

717.2419. 'H NMR is consistent with the structure of the product.

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## Example 10

hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5yl]phenoxy]ethoxy]ethyl]pyridinium 1-[2-[2-[4-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-

5 5 (d, J = 6.0 Hz, 1H). HRMS (ES) Calc'd for  $C_{27}H_{54}N_{3}O_{6}S$ : 668.3733. Found: Hz, 2H), 7.83 (d, J = 8.7 Hz, 1H), 7.96-8.01 (m, 2H), 8.63-8.67 (m, 2H), 9.522H), 4.09-4.15 (m, 5H), 5.23-5.27 (m, 2H), 5.70 (s, 1H), 5.97 (d, J = 2.4 Hz, 2.60-2.69 (m, 1H), 2.80 (s, 6H), 2.83 (s, 3H), 3.69-3.72 (m, 4H), 3.83-3.87 (m 0.89-0.97 (m, 6H), 1.19-1.40 (m, 6H), 1.70-1.74 (m, 4H), 2.00-2.10 (m, 1H), yl]phenoxy]ethoxy]ethoxy]ethyl]pyridinium as a solid. H NMR (CDCl3) & 56.8 mg of 1-[2-[2-[4-[(4R,5R)-3,3-dibutyl-7- (dimethylamino)-2,3,4,5concentrated to form a residue. The residue was triturated with ether to give of pyridine was heated at 70 °C for 16 hours. The reaction mixture was 1H), 6.50 (dd, J = 2.4, 8.8 Hz, 1H), 6.93 (d, J = 8.8 Hz, 2H), 7.46 (d, J = 8.7tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-A solution of 75 mg of the solid prepared in Example 9 above in 5 mL

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Example 11

2-[2-[2-[4-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4yl]phenoxy]ethoxy]ethoxy]-N,N,N-triethylethanaminium iodide hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-

2H), 7.83 (d, J = 8.7 Hz, 1H). HRMS (ES) Calc'd for C<sub>18</sub>H<sub>66</sub>N<sub>3</sub>O<sub>6</sub>S: 690.4516. was used in place of pyridine and heating was at 90 °C for 6 hours. 'H NMR is 1.12-1.45 (m, 15H), 1.60-1.73 (m, 4H), 2.09-2.11 (m, 1H), 2.52-2.55 (m, 1H), The procedure of Example 10 was followed except that triethylamine 2.82 (s, 6H), 2.83 (s, 3H), 3.06-3.15 (m, 2H), 3.53 (q, J = 7.2 Hz, 6H), 3.74consistent with the desired product. 'H NMR (CDCI,) & 0.90-0.97 (m, 6H), 1H), 6.50 (d, J = 3.0 Hz, 1H), 6.93 (d, J = 8.7 Hz, 2H), 7.45 (d, J = 8.7 Hz, 3.75 (m, 4H), 3.86-3.89 (m, 2H), 4.04-4.16 (m, 5H), 5.70 (s, 1H), 5.98 (m, Found: 690.4548. 2

Example 12

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide .12

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3-methoxybenzyl chloride was substituted for 3-nitrobenzyl chloride. 1H NMR The procedures set forth in Example 1 above were followed except that (d, J=2.4 Hz, 1H), 6.50 (dd, J=2.4, 8.4 Hz, 1H), 6.86-6.89 (m, 1H), 7.05 (br was consistent with the product. 'H NMR (CDCI,) & 0.90-0.97 (m, 6H), 1.17-(s, 6H), 2.84 (s, 3H), 3.82 (s, 3H), 4.15 (d, J = 7.8 Hz, 1H), 5.72 (s, 1H), 6.01 1.38 (m, 8H),1.69-1.73 (m, 2H), 2.04-2.08 (m, 1H), 2.55-2.62 (m, 1H), 2.81 s, 1H), 7.13-7.16 (m, 1H), 7.32 (t, J=8.1 Hz, 1H), 7.83 (d, J=8.7 Hz, 1H). MS (M+H\*) 489.

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(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide and (4S,5R)-3,3-dibutyl-7-

Step 1. N-[1-Butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]benzenesulfonamide

mL of  $1.6\,\mathrm{M}$  n-butyllithium in hexane. The reaction mixture was stirred at 0°C for 30 minutes. To the reaction mixture was added 1.9 mL of trimethyl Example 1 above in 10 mL of tetrahydrofuran cooled to 0 °C was added 8.0 To a solution of 2.0 g (4.25 mmol) of the material prepared in Step 4 of

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5 5 chromatography to give 1.72 g of N-[1-butyl-1-[[[(1and concentrated to form a residue. The residue was purified by flash and brine (100 mL). The ethyl acetate layer was dried over magnesium sulfate of ethyl acetate. The ethyl acetate solution was washed with water (100 mL) for 16 hours. The reaction mixture was concentrated and dissolved in 100 mL nitrobenzaldehyde. The ethanol solution was added to the toluene solution to form a residue. The residue was dissolved in 7 mL of ethanol and degassed and the solution extracted. The ethyl acetate layer was washed with water hydrochloric acid to bring the solution to a pH of 6-7 and then the volatiles dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3followed by 10 mL of 1 M aqueous sodium carbonate. The reaction mixture tetrakis(triphenylphosphine)palladium(0), 10 mL of toluene and 918 mg of 3with nitrogen. In a separate flask was placed 150 mg of (100 mL) and brine (100 mL), dried over magnesium sulfate and concentrated were evaporated. To the aqueous solution was added 100 mL of ethyl acetate borate and the mixture stirred 10 minutes at 0 °C and then one hour at room was heated to reflux for one hour, cooled to room temperature, and then stirred temperature. To the reaction mixture was added 100 mL of water and 5%

20 Step 2. N-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(3nitrophenyl)methyl]benzenesulfonamide

nitrophenyl)methyl]benzenesulfonamide.

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The procedure of Step 8 of Example 1 was followed except that N-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4(dimethylamino)-2-[(3-nitrophenyl)methyl]benzenesulfonamide was used in place of N-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide.

Step 3. N-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl) methyl]benzenesulfonamide

To a solution of 79 µL of oxalyl chloride in 2 mL of dichloromethane cooled to -78 °C was added 107 µL of dimethylsulfoxide and the mixture stirred 20 minutes. To the cooled reaction mixture was added a solution of 370 mg (0.75 mmol) of the alcohol from Step 2 above in 2 mL of dichloromethane and the mixture was stirred one hour at -78 °C. To the cooled reaction mixture was added 660 µL of diisopropylethylamine. The reaction mixture was warmed to room temperature and stirred for 30 minutes. To the reaction mixture was added 100 mL of water and mixture was extracted with dichloromethane (2 x 50 mL). The combined dichloromethane layers were washed with him /50 ml. Add over mannerium culfate and

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15 To the reaction mixture was added 100 mL of water and mixture was extracted with dichloromethane (2 x 50 mL). The combined dichloromethane layers were washed with brine (50 mL), dried over magnesium sulfate and concentrated to give 0.47 g of a yellow oil. The residue was dissolved in 25 mL of 25% ethyl acetate in hexane and filtered through silica and concentrated. The residue was crystallized with ethyl acetate and hexane to

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give 301.6 mg of N-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]benzenesulfonamide as a yellow solid.

Step 4. (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide and (45,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

To a solution of 150 mg (0.31 mmol) of the material prepared in Step 3 above in 6 mL of tetrahydrofuran cooled to -15 °C was added 0.90 mL 1 M of potassium t-butoxide in tetrahydrofuran. The reaction mixture was stirred for

- 15 minutes at -15 °C and then water was added. The organics were evaporated and 100 mL of ethyl acetate was added and then extracted. The ethyl acetate layer was washed with brine (100 mL), dried over magnesium sulfate and concentrated to form a residue. The residue was purified by flash chromatography with 30% ethyl acetate in hexane as eluent to give 61.8 mg of (4S,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide, and 65.7 mg of (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide, ¹H NMR and mass spectra were consistent with the product.
- Example 14
- 20 (4R,5R)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-1,2-benzothiazepin 4-ol 1,1-dioxide

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The procedure of Example 2 above was followed except that (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide was used in place of (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide. <sup>1</sup>H NMR was consistent with the product. MS (M') 460.

## Example 15

5-bromo-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl)phenyl]pentanamide

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The procedure of Example 3 above was followed except that (4R,5R)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-1,2-benzothiazepin-4-ol 1,1-dioxide was used in place of (4R,5R)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide. ¹H NMR was consistent with the product. MS (M+H\*) 623.

## Example 16

5-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-N,N,N-triethyl-5-oxo-1-pentanaminium trifluoroacetate

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To a solution of 54.1 mg (0.09 mmol) of the bromide prepared in Example 15 above in 1 mL of tetrahydrofuran was added 48 µL of triethylamine. The reaction mixture was heated at reflux for three days. The solvent was evaporated and the residue triturated with ether. The solid was purified by reverse phase high pressure liquid chromatography to give 17.9 mg of 5-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazzepin-5-yl]phenyl]amino]-N,N,N-triethyl-

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5-oxo-1-pentanaminium trifluoroacetate as a white solid. <sup>1</sup>H NMR was consistent with the product. MS (M\*) 643.

Example 17

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-phenyl-1,2-

benzothiazepin-4-ol 1,1-dioxide

Step 1-2. N-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-(phenylmethyl)benzenesulfonamide

The procedure of Steps 1-2 of Example 7 was followed except that N-[[(1,1 dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-

(dimethylamino)benzenesulfonamide and benzyl chloride were used in place of N-[1-butyl-1-[[[(1,1dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-N-methylbenzenesulfonamide and p-methoxybenzyl

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chloride.

Step 3. N-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-(phenylmethyl) benzenesulfonamide

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The procedure of Step 3 of Example 13 was followed except that N-[1-

butyl-1-(hydroxymethyl)pentyl] 4-(dimethylamino)-2-(phenylmethyl)
benzenesulfonamide was used in place of N-[1-butyl-1-(hydroxymethyl)
pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]benzenesulfonamide.

Step 4. (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-phenyl-1,2-benzothiazzepin-4-ol 1,1-dioxide 10 The procedure Step 4 of Example 7 was followed except that N-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-(phenylmethyl)
benzenesulfonamide was used in place of N-[1-butyl-1-formylpentyl]-4(dimethylamino)-2-[(4-methoxyphenyl)methyl]-N-methylbenzenesulfonamide. 'H NMR (CDCI<sub>3</sub>) 8 0.9 (m, 6H), 1-1.7 (m, 13H), 2.3 (m, 1H),
15 2.8 (s, 6H), 4.0 (s, 2H), 5.5 (s, 1H), 5.9 (s, 1H), 6.5 (m, 1H), 7.4 (m, 3H), 7.5

(m, 2H), 7.8 (m, 1H). MS (M+H+) 445.0.

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Example 18

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

Step 1. N-[1-Butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[[4-methoxyphenyl)methyl]benzenesulfonamide

The procedure of Step 1 of Example 7 was followed except that N-[1-butyl-1-[[[(1,1dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)benzenesulfonamide was used in place of N-[1-butyl-1-[[[((1,1dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-N-methylbenzenesulfonamide.

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Step 2. N-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]benzenesulfonamide

The procedure of Step 8 of Example 1 was followed except that N-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]benzenesulfonamide was used in place of N-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl] pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide.

Step 3. N-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl) 10 methyl]benzenesulfonamide

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The procedure of Step 3 of Example 13 was followed except that N-[1-butyl-1-(bydroxymethyl)pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl) methyl]benzenesulfonamide was used in place of N-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide.

Step 4. (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

The procedure of Step 10 of Example 1 was followed except that N-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl] benzenesulfonamide was used in place of N-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide. ¹H NMR (CDC1<sub>1</sub>) 8 0.89-1.00 (m, 6H), 1.06-1.73 (m, 11H), 2.36 (t, J = 9.5 Hz, 1H), 2.80 (s, 6H), 2.98 (s, 1H), 3.85 (s, 3H), 3.97 (s, 1H), 4.03 (d, J = 9.0 Hz, 1H), 5.47 (s, 1H), 6.00 (d, J = 2.4 Hz, 1H), 6.50 (dd, J = 2.6, 8.9 Hz, 1H), 6.95 (d, J = 8.8 Hz, 2H), 7.44 (d, J = 8.5 Hz, 2H), 7.81 (d, J = 8.7 Hz, 1H).

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## Example 19

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(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

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The procedure set forth in Example 8 above was followed except that (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide was used in place of (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-2-methyl-1,2-

benzothiazepin 4-ol 1,1-dioxide and a reaction temperature of 0 °C was employed. ¹H NMR (CDCl<sub>3</sub>) 8 0.86-0.97 (m, 6H), 1.15-1.75 (m, 11H), 2.35 (t, J = 9.9 Hz, 1H), 2.80 (s, 6H), 3.98 (s, 1H), 4.02 (d, J = 8.6 Hz, 1H), 5.12 (s, 1H), 5.45 (s, 1H), 5.98 (d, J = 2.4 Hz, 1H), 6.48 (dd, J = 2.6, 8.6 Hz, 1H), 6.88 (d, J = 8.8 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 7.80 (d, J = 8.7 Hz, 1H).

10 Example 20

2-[2-[2-[4-[(4R,SR)-3,3-dibutyl-7- (dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-y]phenoxy]ethoxy]ethoxy]-N,N,N-triethylethanaminium iodide

Step 1

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The procedure set forth in Example 9 above was followed except that

- hydroxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide was used in place of (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-((2-4R,5R)-3,3-4))equivalents. 'H NMR was consistent with the product. dioxide and 3.3 equivalents of 95% sodium hydride was used instead of 2.2 iodoethyoxy)ethoxy)phenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-
- 10 N,N,N-triethylethanaminium iodide 4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]-

0.88-0.05 (m, 6H), 1.14-1.60 (m, 20H), 2.31-2.39 (m, 1H), 2.82 (s, 6H), 3.06the benzothiazepine prepared in Step 1 above was used. <sup>1</sup>H NMR (CDCl<sub>3</sub>) & The procedure set forth in Example 10 above was followed except that

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Step 2. 2-[2-[4-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-

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5.47 (s, 1H), 5.98-6.02 (m, 1H), 6.47-6.54 (m, 1H), 6.93-6.98 (m, 2H), 7.42-3.15 (m, 2H), 3.54 (q, J = 7.3 Hz, 6H), 3.75-3.81 (m, 4H), 3.88-4.17 (m, 7H),7.47 (m, 2H), 7.81-7.84 (m, 1H).

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

benzenesulfonamide (dimethylamino)-2-[(3-nitrophenyl)methyl]-N-(phenylmethyl) Step 1. N-[1-Butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-

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To a solution of 4.24 g (7.0 mmol) of the sulfonamide prepared in Step 1 of Example 13 in 30 mL of acctone was added 2.90 g of potassium carbonate, 0.517 g of tetra-n-butylammonium iodide then 2.394 g of benzyl bromide. The reaction mixture was heated at reflux for five daya. To the reaction mixture was added 2.394 g of benzyl bromide, 0.517 g of tetra-n-butylammonium iodide, and then 2.90 g of powdered potassium carbonate. The reaction mixture was heated at reflux for one day. To the reaction mixture 250 mL of ethyl acetate was added. The ethyl acetate solution was washed with water (3 x 100 mL) and brine (200 mL). The ethyl acetate layer was

dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-(phenylmethyl)benzenesulfonamide.

dried over magnesium sulfate and concentrated to a residue. The residue was

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purified by flash chromatography to give 1.82 g of N-[1-butyl-1-[[[(1-

Step 2. N-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(3-15 nitrophenyl)methyl]-N-(phenylmethyl)benzenesulfonamide

The procedure of Step 8 of Example 1 was followed except that N-[1-butyl-1-[[((1-dimethyl)thyl)dimethyl]loxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl]methyl]-N-(phenylmethyl) benzenesulfonamide was used in place of N-[1-butyl-1-[[[(1-

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dimethylethyl)dimethylsilyl)oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide.

Step 3. N-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-(phenylmethyl)benzenesulfonamide

The procedure of Step 3 of Example 13 was followed except that N-[1-Butyl-1-(thydroxymethyl)pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl) methyl]-N-(phenylmethyl)benzenesulfonamide was used in place of N-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]benzenesulfonamide.

Step 4. (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

The procedure of Step 10 of Example 1 was followed except that N-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-(phenylmethyl)benzenesulfonamide was used in place of N-[1-butyl-1-15 formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide. <sup>1</sup>H NMR was consistent with the product. MS (M+H') 580.

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Example 22

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-5-[3-(ethylamino)phenyl]-2,3,4,5tetrahydro-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

4 of Example 21 in 50 mL ethanol was added about 10 mg of Pearlman's  $(CDCl_1)$   $\delta$  0.72 (t, J = 6.6, 3H), 0.90 (t, J = 7.4 Hz), 1.00-1.98 (m, 15H), 2.81 was dried over magnesium sulfate and concentrated to give 39.8 mg of a washed with water (2 x 50 mL) and brine (50 mL). The ethyl acetate layer Catalyst. This mixture was hydrogenated at 60 psi H<sub>2</sub> for 20 hours. To the 6.83 (m, 1H), 6.95-7.00 (m, 1H), 7.16-7.31 (m, 5H), 7.40 (d, J = 7.2 Hz, 1H), (s, 6H), 3.17 (q, J = 7.2 Hz, 2H), 4.15 (d, J = 7.8 Hz, 1H), 4.39 (s, 2H), 5.69residue. The residue was purified by flash chromatography to give 12.6 mg of mixture was filtered and washed with 50 mL of ethyl acetate. The filtrate was mixture was hydrogenated at 60 psi at 60 °C for 20 hours. The reaction reaction mixture was added about 10 mg of Pearlman's Catalyst and the 7.81 (d, J = 8.7 Hz, 1H). MS (M+H\*) 578. (s, 1H), 6.12 (s, 1H), 6.47 (dd, J = 2.7, 9.0 Hz, 1H), 6.61-6.65 (m, 1H), 6.78tetrahydro-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide. 1H NMR (4R,5R)-3,3-dibutyl-7-(dimethylamino)-5-[3-(ethylamino)phenyl]-2,3,4,5-To a solution of 50 mg (0.09 mmol) of the compound prepared in Step

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Example 23

(4R,SR)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

Step 1. N-[1-Butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-45 (dimethylamino)-2-[(4-methoxyphenyl)methyl]-N(phenylmethyl)benzenesulfonamide

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To a solution of 2.15 g (4.05 mmol) of the sulfonamide prepared in Step 1 of Example 7 above in 30 mL of dimethylformamide was added 123 mg of 95% sodium hydride and then 964 µL of benzyl bromide. The reaction mixture was stirred 18 hours. To the reaction mixture was added 250 mL of ethyl acetate and the mixture was washed with saturated sodium bicarbonate solution (100 mL) and brine (150 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated to give 2.88 g of N-[1-butyl-1-[[[(1-dimethylehyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-N-(phenylmethyl)benzenesulfonamide.

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Step 2. N-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-N-(phenylmethyl)benzenesulfonamide

The procedure of Step 8 of Example 1 was followed except that N-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-

15 (dimethylamino)-2-[(4-methoxyphenyl)methyl]-N-

(phenylmethyl)benzenesulfonamide was used in place of N-[1-butyl-1-[[[(1-dimethyl)thyl)dimethylsily]]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide.

Step 3. N-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-

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nitrophenyl)methyl]-N-(phenylmethyl)benzenesulfonamide

The procedure of Step 3 of Example 13 was followed except that N-[1-

butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(4-

methoxyphenyl)methyl]-N-(phenylmethyl)benzenesulfonamide was used in place of N-[1-butyl-1-{[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide.

Step 4. (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

10 The procedure of Step 10 of Example 1 was followed except that N-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N- (phenylmethyl)benzenesulfonamide was used in place of N-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N- methylbenzenesulfonamide. 'H NMR (CDCl<sub>3</sub>) 8 0.7 (m, 3H), 0.9 (m, 3H), 1-

15 1.7 (m, 10H), 1.9 (m, 1H), 2.1 (m, 1H), 2.8 (s, 6H), 3.8 (s, 3H), 4.1 (s, 1H), 4.4 (s, 2H), 5.8 (s, 1H), 6.0 (s, 1H), 6.5 (m, 1H), 7.0 (d, J=8 Hz, 1H), 7.1-7.5 (m, 7H), 7.8 (m, 1H).

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(4R,5R)-7-dimethylamino)-2-ethyl-4,5-dihydro-5-(4-methoxyphenyl)-spiro[1,2-benzothiazepine-3(2H),1'-cyclopentan]-4-ol 1,1-dioxide

Step 1. N-[1-(hydroxymethyl)cyclopentyl]-4-fluorobenzenesulfonamide

The procedure of Step 2 of Example 1 was followed except that cycloleucinol was substituted for 2-amino-2-butylhexanol.

The procedure of Steps 3 and 4 of Example 1 was followed except that

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N-[1-(hydroxymethyl)cyclopentyl]-4-fluorobenzenesulfonamide was used in place of <math>N-[1-butyl-1-(hydroxymethyl)pentyl]-4-fluorobenzenesulfonamide.

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Step 4. N-[1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]cyclopentyl]-4- (dimethylamino)-2-[(4-methoxyphenyl)methyl]-N-methylbenzenesulfonamide

The procedure of Step 1 of Example 7 was followed except that N-[1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]cyclopentyl]-4-(dimethylamino)benzenesulfonamide was used in place of N-[1-butyl-1-[[[(1,1dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-N-methylbenzenesulfonamide.

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Step 5. N-[1-(hydroxymethyl)cyclopentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-N-ethylbenzenesulfonamide

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To a solution of 0.25 g (0.49 mmol) of the sulfonamide prepared in Step 4 above in 5 mL of tetrahydrofuran was added 25 mg of 95% sodium hydride. After 15 minutes, 125 µL of ethyl iodide was added to the reaction mixture was stirred 16 hours. To the reaction mixture was added 5 mL of dimethylformamide and the mixture stirred four hours. To the reaction mixture was added 5 mL of dimethylformamide and the mixture stirred four hours. To the reaction mixture 100 mL of water was added and the mixture extracted with 100 mL of ethyl acetate. The ethyl acetate layer was washed with brine (100 mL), dried over magnesium sulfate and concentrated to give 0.27g of an

10 Step 6-8. (4R,5R)-7-dimethylamino)-2-ethyl-4,5-dihydro-5-(4-methoxyphenyl)-spiro[1,2-benzothiazepino-3(2H),1'-cyclopentan]-4-ol 1,1-dioxide

o:

The procedure of Steps 8-10 of Example 1 was followed except that N-[1-(hydroxymethyl)cyclopentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-N-ethylbenzenesulfonamide was used in place of N-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-N-methylbenzenesulfonamide. ¹H NMR was consistent with product. MS (M+H\*) 445.

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## Biological Assays

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The utility of the compounds of the present invention is shown by the following assays. These assays are performed in vitro and in animal models essentially using a procedure recognized to show the utility of the present invention.

In Vitro Assay Of Compounds That Inhibit IBAT-Mediated Uptake Of IMCI-

25 Taurocholate (TC) in H14 Cells

Baby hamster kidney cells (BHK) transfected with the cDNA of

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human IBAT (H14 cells) are seeded at 60,000 cells/well in 96 well Top-Count tissue culture plates for assays run within 24 hours of seeding; 30,000 cells/well for assays run within 48 hours; and 10,000 cells/well for assays run within 72 hours.

- On the day of assay, the cell monolayer is gently washed once with 100 mL assay buffer (Dulbecco's Modified Eagle's medium with 4.5 g/L glucose + 0.2% (w/v) fatty acid free bovine serum albumin ((FAF)BSA). To each well 50 mL of a two-fold concentrate of test compound in assay buffer is added along with 50 mL of 6 mM [<sup>14</sup>C]-laurocholate in assay buffer (final
- oconcentration of 3 mM [<sup>14</sup>C]-taurocholate). The cell culture plates are incubated two hours at 37° C prior to gently washing each well twice with 100 mL of 4° C Dulbecco's phosphate-buffered saline (PBS) containing 0.2% (w/v) (FAF)BSA. The wells are then gently washed once with 100 mL of 4° C PBS without (FAF)BSA. To each 200 mL of liquid scintillation counting fluid is
  - 15 added, the plates are heat sealed and shaken for 30 minutes at room temperature prior to measuring the amount of radioactivity in each well on a Packard Top-Count instrument.

In Vitro Assay Of Compounds That Inhibit Uptake Of I"CI-Alanine

The alanine uptake assay is performed in an identical fashion to the

20 taurocholate assay, with the exception that labeled alanine is substituted for the labeled taurocholate. Data from each of the noted compounds in this assay is as set forth in Table 4 below:

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Table 4

	COMPOUND	HUMAN TC IC <sub>50</sub>	ALANINE UPTAKE
	(EXAMPLE	(μM)	IC,
	NUMBER)		
5	1	1.2	
	2	0.32	
	3	0.69	
	4	0.083	>100
	5	0.97	
0	6	0.32	
	7	0.57	
	8	0.58	
	10	0.31	
	11	0.20	
S	12	1.2	
	13 (cis)	0.044	
	13 (trans)	0.21	
	14	0.006	
	15	0.022	
0	16	0.0016	
	17	0.035	
	18	0.026	
	19	0.003	>100
	20	0.008	
ίλ	21		>1.0
	22	2.5	
	24	130	

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# In Vivo Assay Of Compounds That Inhibit Rat Ileal Uptake Of ["Cl-

Taurocholate into Bile

(See "Metabolism of 3α,7βdihydroxy-7β-methyl-5β-cholanoic acid and 3α,7β-dihydroxy-7α-methyl-5β-cholanoic acid in hamsters" in Biochimica et Biophysica Acta 833 (1985) 196-202 by Une et al.)

and the cecum. A slit is cut at 4 cm from this same junction (utilizing a 8 cm mL of control sample ([14C]-taurocholate @ 0.05 mi/mL with 5 mM cold 6.5 (PBS) is used to flush out the intestine segment. The distal opening is exposed and laid out on a gauze pad. A canulae (1/8" luer lock, tapered ducts are cannulated with a 10" length of PE10 tubing. The small intestine is Male wistar rats (200-300 g) are anesthetized with inactin @100 mg/kg. Bile minutes for the first 27 minutes of the procedure. After the 21 minutes of mL/minute for 21 minutes. Bile samples fractions are collected every three taurocholate) is loaded into the gut segment with a 3 mL syringe and bile the gut segment is monitored continuously. At the start of the experiment, 2.0 washed for 20 minutes with warm PBS at 0.25 mL/minute. Temperature of The proximal cannulae is hooked up to a peristaltic pump and the intestine is cannulated with a 20 cm length of silicone tubing (0.02" I.D. x 0.037" O.D.). length of ileum). 20 mL of warm Dulbecco's phosphate buffered saline, pH female adapter) is inserted at 12 cm from the junction of the small intestine sample collection is begun. Control sample is infused at a rate of 0.25.

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sample infusion, the iteal loop is washed out with 20 mL of warm PBS (using a 30 mL syringe), and then the loop is washed out for 21 minutes with warm PBS at 0.25 mL/minute. A second perfusion is initiated as described above but with the test compound being administered as well (21 minutes administration followed by 21 minutes of wash out) and bile sampled every three minutes for the first 27 minutes. If necessary, a third perfusion is performed as above that typically contains the control sample.

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Measurement Of Hepatic Cholesterol Concentration (HEPATIC CHOL.)

Liver tissue is weighed and homogenized in chloroform:methanol (2:1). After homogenization and centrifugation the supernatant is separated and dried under nitrogen. The residue is dissolved in isopropanol and the cholesterol

content is measured enzymatically, using a combination of cholesterol oxidase and peroxidase, as described by Allain, C. A., et al. (1974) Clin. Chem. 20,

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# Measurement Of Hepatic HMG CoA-Reductase Activity (HMG COA)

Hepatic microsomes are prepared by homogenizing liver samples in a

phosphate/sucrose buffer, followed by centrifugal separation. The final
pelleted material is resuspended in buffer and an aliquot is assayed for HMG

CoA reductase activity by incubating for 60 minutes at 37° C in the presence of "C-HMG-CoA (Dupont-NEN). The reaction is stopped by adding 6N HCl

followed by centrifugation. An aliquot of the supernatant is separated, by thin15 layer chromatography, and the spot corresponding to the enzyme product is
scraped off the plate, extracted and radioactivity is determined by scintillation
counting, (Reference: Akerlund, J. and Bjorkhem, I. (1990) J. Lipid Res. 31,

Determination Of Serum Cholesterol (SER, CHOL, HDL-CHOL, TGI and

20 VLDL+LDL)

Total serum cholesterol (SER.CHOL) is measured enzymatically using a commercial kit from Wako Fine Chemicals (Richmond, VA); Cholesterol C11, Catalog No. 276-64909. HDL cholesterol (HDL-CHOL) is assayed using this same kit after precipitation of VLDL and LDL with Sigma

25 Chemical Co. HDL Cholesterol reagent, Catalog No. 352-3 (dextran sulfate method). Total serum triglycerides (blanked) (TGI) are assayed enzymatically with Sigma Chemical Co. GPO-Trinder, Catalog No. 337-B. VLDL and LDL

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(VLDL + LDL) cholesterol concentrations are calculated as the difference between total and HDL cholesterol.

Measurement Of Hepatic Cholesterol 7-a Hydroxylase Activity (7a-OHase)

Hepatic microsomes are prepared by homogenizing liver samples in a phosphate/sucrose buffer, followed by centrifugal separation. The final pelleted material is resuspended in buffer and an aliquot is assayed for cholesterol 7-a-hydroxylase activity by incubating for 5 minutes at 37° C in the presence of NADPH. Following extraction into petroleum ether, the organic solvent is evaporated and the residue is dissolved in acetonitrile/

10 methanol. The enzymatic product is separated by injecting an aliquot of the extract onto a C<sub>11</sub> reversed phase HPLC column and quantitating the eluted material using UV detection at 240mm. (Reference: Horton, J. D., et al. (1994) J. Clin. Invest. 93, 2084).

Rat Gayage Assay

Male Wister rats (275-300g) are administered IBAT inhibitors using an oral gavage procedure. Drug or vehicle (0.2% Tween 80 in water) is administered once a day (9:00-10:00 a.m.) for four days at varying dosages in a final volume of 2 mL per kilogram of body weight. Total fecal samples are collected during the final 48 hours of the treatment period and analyzed for

20 bile acid content using an enzymatic assay as described below. Compound efficacy is determined by comparison of the increase in fecal bile acid (FBA) concentration in treated rats to the mean FBA concentration of rats in the vehicle group. Table 5 describes the results of this assay when the compound of Example 4 was tested.

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Table 5

COMPOUND	DOSE (mg/kg/day)	% INCREASE IN
(EXAMPLE		FECAL BILE ACID
NUMBER)		CONCENTRATION
4	5	217.2
4	0.4	157.8
4	0.04	244.0

## Measurement Of Fecal Bile Acid Concentration (FBA)

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Total fecal output from individually housed hamsters is collected for 24 or 48 hours, dried under a stream of nitrogen, pulverized and weighed. Approximately 0.1 gram is weighed out and extracted into an organic solvent (butanol/water). Following separation and drying, the residue is dissolved in methanol and the amount of bile acid present is measured enzymatically using the 3\alpha-hydroxysteroid steroid dehydrogenase reaction with bile acids to reduce NAD. (Reference: Mashige, F., et al. (1981) Clin. Chem. 27, 1352).

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# (\*Hitaurocholate Uptake in Rabbit Brush Border Membrane Vesicles (BBMY)

Rabbit Ileal brush border membranes are prepared from frozen ileal mucosa by the calcium precipitation method described by Malathi et al. (Reference: (1979) Biochimica Biophysica Acta, 554, 259). The method for

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- (Reference: (1979) Biochimica Biophysica Acta, 554, 259). The method for measuring taurocholate is essentially as described by Kramer et al. (Reference: (1992) Biochimica Biophysica Acta, 1111, 93) except the assay volume is 200 µL instead of 100 µL. Briefly, at room temperature a 190 µL solution containing 2µM [³H]-taurocholate(0.75 µCi), 20 mM tris, 100 mM NaCl, 100
- 25 mM mannitol pH 7.4 is incubated for 5 seconds with 10 μL of brush border membrane vesicles (60-120 μg protein). The incubation is initiated by the addition of the BBMV while vortexing and the reaction is stopped by the

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addition of 5 mL of ice cold buffer (20 mM Hepes-tris, 150 mM KCl) followed immediately by filtration through a nylon filter (0.2 µm pore) and an additional 5 mL wash with stop buffer.

## Acyl-CoA; cholesterol Acyl Transferase (ACAT)

20 2 ಠ with similar success by substituting the generically or specifically described preceding examples TLC plate with a Packard instaimager. The examples herein can be repeated The amount of cholesterol ester formed is determined by measuring the spotted on a silica gel 60 TLC plate and developed in hexane/ethyl ether (9:1). thorough vortexing. The chloroform phase is taken to dryness and then and aqueous phases of the extraction are separated by centrifugation after cholesterol oleate in chloroform methanol to act as a carrier and the organic of chloroform/methanol (2:1). To the extraction is added 125 µg of protein. The assay is initiated by the addition of oleoyl-CoA. The reaction reactants and/or operating conditions of this invention for those used in the amount of radioactivity incorporated into the cholesterol oleate spot on the proceeds for five minutes at 37° C and is terminated by the addition of 8.0 mL mM DTT ph 7.4 buffer containing 0.25 % BSA and 200 µg of microsomal containing 24 µM Oleoyl-CoA (0.05 µCi) in a 50 mM sodium phosphate, 2 a source of ACAT enzyme. The assay consists of a 2.0 mL incubation described previously (Reference: (1980) J. Biol. Chem. 255, 9098) and used as Hamster liver and rat intestinal microsomes are prepared from tissue as

The invention being thus described, it is apparent that the same can be varied in many ways. Such variations are not to be regarded as a departure from the spirit and scope of the present invention, and all such modifications and equivalents as would be obvious to one skilled in the art are intended to be included within the scope of the following claims.

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1. A compound of formula (I):

wherein:

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q is an integer from 1 to 4;

15 R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of hydrogen and hydrocarbyl, wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus;

R<sup>3</sup> and R<sup>4</sup> are independently selected from the group consisting of hydrogen; hydrocarbyl; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; and -SO<sub>3</sub>R<sup>9</sup>; or

 $R^3$  and  $R^4$  together form =0; =NOR $^9$ ; =S; =NNR $^9$ R $^{10}$ ; =NR $^9$ , or =CR $^{11}$ R $^{12}$ ;

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wherein R<sup>9</sup> and R<sup>10</sup> are independently selected from the group consisting of hydrogen; hydrocarbyl; amino; and hydrocarbylamino; wherein said hydrocarbyl moeities may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl moieties optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; and

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wherein R<sup>11</sup> and R<sup>12</sup> are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; hydrocarbyl; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO2R<sup>9</sup>; and -SO3R<sup>9</sup>; wherein said hydrocarbyl moeities may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl moieties optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus;

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 $R^{11}\,\mathrm{and}\,R^{12}$  together with the carbon atom to which they are attached form a cyclic ring; and

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R<sup>5</sup> and R<sup>6</sup> are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; -OR<sup>2</sup>; -S(O)R<sup>2</sup>; -SO<sub>2</sub>R<sup>2</sup>; and -SO<sub>3</sub>R<sup>2</sup>;

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wherein the R<sup>5</sup> and R<sup>6</sup> radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen;
-NO<sub>2</sub>; -CN; oxo; hydrocarbyl; -OR<sup>13</sup>; -NR<sup>13</sup>; -NR<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO<sub>2</sub>R<sup>13</sup>; -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>OM; -CO<sub>3</sub>NR<sup>13</sup>R<sup>14</sup>; -C(O)NR<sup>13</sup>R<sup>14</sup>; -C(O)OM; -COR<sup>13</sup>;

wherein R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> are independently selected from the group consisting of hydrogen or hydrocarbyl, wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heterostoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heterostoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; or

wherein R<sup>13</sup> and R<sup>14</sup> together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally

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oxo, carboxy, and quaternary salts; or substituted with one or more radicals selected from the group consisting of

are attached form a cyclic ring; and wherein  $\mathbb{R}^{14}$  and  $\mathbb{R}^{15}$  together with the nitrogen atom to which they

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pharmaceutically acceptable cation; and wherein A is a pharmaceutically acceptable anion, and M is a

wherein R9 is as defined above; or

R4 and R6 together represent a bond; and

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optionally may have one or more carbon atoms replaced by one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl wherein said hydrocarbyl may be optionally substituted with one or more heteroatoms independently selected from the group consisting of oxygen,  $\mathbb{R}^N$  is selected from the group consisting of hydrogen and hydrocarbyl,

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nitrogen, sulfur and phosphorus;

consisting of hydrogen; halogen; -CN; -NO2; hydrocarbyl; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>A; -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -S(O)2R<sup>13</sup>; -SO3R<sup>13</sup>; -S<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO2R<sup>13</sup>; -OM; -SO2OM; -SO2NR<sup>13</sup>R<sup>14</sup>. one or more RX radicals are independently selected from the group

 $\begin{array}{l} NR^{1}C(O)R^{13}, -C(O)NR^{13}R^{14}, -C(O)OM; -COR^{13}, -S(O)_{h}NR^{13}R^{14}, -N^{13}R^{14}R^{15}A^{-}; -PR^{13}R^{14}, -P(O)R^{13}R^{14}; -P^{13}R^{14}R^{15}A^{-}; \ amino \ acid \\ \end{array}$ wherein said hydrocarbyl may be optionally substituted with one or more residue; peptide residue; polypeptide residue; and carbohydrate residue, groups comprising one or more heterostoms, and wherein said hydrocarby

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nitrogen, sulfur and phosphorus; and wherein n is 0, 1 or 2; and

heteroatoms independently selected from the group consisting of oxygen optionally may have one or more carbon atoms replaced by one or more

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wherein R13, R14, R15, A, and M are as defined above; or

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other than hydrogen or alkyl; and provided that at least one of  $\mathbb{R}^1$ ,  $\mathbb{R}^2$ ,  $\mathbb{R}^3$ ,  $\mathbb{R}^4$ ,  $\mathbb{R}^5$ , and  $\mathbb{R}^6$  is a radical a pharmaceutically acceptable salt, solvate, or prodrug thereof; and

provided that when R<sup>5</sup> or R<sup>6</sup> is aryl, the other of R<sup>2</sup> and R<sup>6</sup> is a radical

other than heterocycylalkyl.

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2. A compound of claim 1 wherein:

q is an integer from 1 to 4;

arylaikyl; heterocyclylaikyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; hydrogen; alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; R and R are independently selected from the group consisting of

heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl;

form C3-C10 cycloalkyl or C3-C10 cycloalkenyl;  $\mathbb{R}^1$  and  $\mathbb{R}^2$  taken together with the carbon to which they are attached

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alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; wherein the R1 and R2 alkyl; cycloalkyl; alkenyl; cycloalkenyl;

ᅜ  $OR^9$ ;  $.NR^9R^{10}$ ;  $.N^+R^9R^{10}R^WA^-$ ;  $.SR^9$ ;  $.S^*R^9R^{10}A^-$ ;  $.PR^9R^{10}$ ; and  $.S^+R^9R^{10}R^WA^-$ ;  $.S(0)R^9$ ;  $.SO_2R^9$ ;  $.SO_3R^9$ ;  $.SO_2R^9$ ; and  $.SO_3R^9$ ; .SOor more radicals selected from the group consisting of -CN; halogen; oxo; alkylaryl; and (polyalkyl)aryl radicals optionally may be substituted with one wherein the R1 and R2 alkyl; cycloalkyl; alkenyl; cycloalkenyl;

ટ 8 PR9-; -P(O)R9-; -P+R9R10A--; or phenylene; and alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkylaryl; and (polyalkyl)aryl radicals optionally may have one or more carbons replaced by -O-; -NR -; -N<sup>+</sup>R <sup>9</sup>R <sup>10</sup>A -; -S-; -SO-; -SO<sub>2</sub>-; -S <sup>+</sup>R <sup>9</sup>A -; heterocylcyloxyalkyi; heterocycloxyalkenyi; heterocyclyloxyalkynyi;

ဗ carboxyalkylamino; alkoxyalkylamino; and acyl; and consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; carboaikoxyalkyl; carboxyaryl; carboxyheterocyclyl; amino; alkylamino; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl wherein R<sup>9</sup>, R<sup>10</sup>, and R<sup>w</sup> are independently selected from the group

S(O)R'; -SO2R'; and -SO3R'; or hydrogen; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -SR<sup>9</sup>; -R3 and R4 are independently selected from the group consisting of wherein A is a pharmaceutically acceptable anion; and

 $\rm R^3$  and  $\rm R^4$  together form =0; =NOR  $^9$  ; =S; =NNR  $^9\rm R_1^0$  ; =NR  $^9\rm ,\, or$ -CR11R12; 33

carboalkoxyalkyl; cycloalkyl; cycloalkenyl; haloalkyl; hydroxyalkyl; cyanoalkyl; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -CO<sub>2</sub>R<sup>9</sup>; consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkynyl; aryl; wherein  $\mathrm{R}^{11}$  and  $\mathrm{R}^{12}$  are independently selected from the group heterocyclyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; and -CONR9R10; or

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 $\mathbb{R}^{11}$  and  $\mathbb{R}^{12}$  together with the carbon atom to which they are attached form a cyclic ring; and

wherein R9 and R10 are as defined above; and

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hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary  $R^{5}$  and  $R^{6}$  are independently selected from the group consisting of heterocyclyl; -OR<sup>9</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; and -SO<sub>3</sub>R<sup>9</sup>;

wherein the  $R^5$  and  $R^6$  alkyl; cycloalkyl; alkenyl; aryl; aryl;

substituted with one or more radicals independently selected from the group hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; SR<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; CO2R<sup>13</sup>, OM; -SO2OM; -SO2NR<sup>13</sup>R<sup>14</sup>; -C(O)NR<sup>13</sup>R<sup>14</sup>; -C(O)OM;  $\cos^{13}$ ; -NR $^{12}$ COR $^{14}$ ; -NR $^{13}$ CO)NR $^{14}$ R $^{15}$ ; -NR $^{13}$ CO,R $^{14}$ ; -OC(O)R $^{13}$ ; heterocyclyl; and quaternary heterocyclyl radicals optionally may be consisting of halogen; -CN; -NO2; oxo; alkyl; polyalkyl; haloalkyl; NR<sup>13</sup>SO,NR'4R'5,-PR<sup>13</sup>R<sup>14</sup>, -P(O)R<sup>13</sup>R<sup>14</sup>,-P<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A;-P(OR<sup>13</sup>)OR<sup>14</sup>;-S<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A'; and -N<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A'; and OC(0)NR11R1; -NR13OR14; -NR13O1R14; -NR13SONR14R13; -S 55 8

optionally may be further substituted with one or more radicals selected from  $\mathsf{heterocyclyl}; -\mathsf{OR}^{\mathcal{I}}; -\mathsf{NR}^{\mathcal{I}}R^3; -\mathsf{SR}^{\mathcal{I}}; -\mathsf{S}(\mathsf{O})R^{\mathcal{I}}; -\mathsf{S}(\mathsf{O}2R^{\mathcal{I}}; -\mathsf{S}(\mathsf{O}3R^{\mathcal{I}}; -\mathsf{S}(\mathsf{O}3R^{\mathcal{I}}; -\mathsf{S}(\mathsf{O}3R^{\mathcal{I}}; -\mathsf{S}(\mathsf{O}3R^{\mathcal{I}); -\mathsf{S}(\mathsf{O}3R^{\mathcal{I}}; -\mathsf{S}$ alkenyi; alkynyi; aryi; heterocyclyi; arylalkyi; heterocyclylalkyi; quaternary wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, CONR<sup>7</sup>R<sup>8</sup>; -N<sup>+</sup>R<sup>7</sup>R<sup>8</sup>R<sup>9</sup>A-; -P(O)R<sup>7</sup>R<sup>8</sup>; -PR<sup>7</sup>R<sup>8</sup>; -P<sup>+</sup>R<sup>7</sup>R<sup>8</sup>R<sup>9</sup>A; and the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl, aikynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R3 and R6 radicals 2(O)(OR')OR'; and

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optionally may have one or more carbons replaced by -O.; -NR7.; -N+R7R8A. -: -S-; -SO-; -SO2-; -S<sup>+</sup>R<sup>7</sup>A-; -P(O)R<sup>7</sup>-; -P<sup>+</sup>R<sup>7</sup>R<sup>8</sup>A-; or phenylene; wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R3 and R6 radicals 뗥 2 23

consisting of hydrogen; alkyl, alkenyl; alkymyl; aryl; and heterocyclyl; and wherein  $\mathbb{R}^7$  and  $\mathbb{R}^8$  are independently selected from the group

wherein  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl;

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heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminoalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or aminocarbonylalkyl; alkylaminocarbonylalkyl;

wherein R13 and R14 together with the nitrogen atom to which they substituted with one or more radicals selected from the group consisting of are attached form a mono- or polycyclic heterocyclyl that is optionally oxo, carboxy, and quaternary salts; or 8

wherein R 14 and R 15 together with the nitrogen atom to which they are attached form a cyclic ring; and

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wherein the R13, R14, and R15 alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quatemary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminoalkyl;

halogen; -CN; sulfo; oxo; alkyl; haloalkyl; hydroxyalkyl; sulfoalkyl; alkenyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of aminocarbonylalkyl; alkylaminocarbonylalkyl; જ

 $N^{+}R^{2}R^{1}0_{R}^{W}A$ ;  $-SR^{16}$ ,  $-S(O)R^{9}$ ,  $-SO_{2}R^{9}$ ;  $-SO_{3}R^{16}$ ,  $-CO_{2}R^{16}$ ;  $-CO_{1}R^{9}R^{10}$ ;  $-SO_{2}NR^{9}R^{10}$ ;  $-PO(OR^{16})OR^{17}$ ;  $-P^{9}R^{10}$ ;  $-P^{+}R^{9}R^{10}R^{11}A$ . heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; -OR16; -NR9R10; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary S<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-; and carbohydrate residue; and 8

200 alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminoalkyl; heterocyclylalkyl; quatemary heterocyclylalkyl; alkylarylalkyl; wherein the R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> alkyl; haloalkyl; cycloalkyl; polyalkyl;

= one or more carbons replaced by -O-; -NR2-; -NTR2 R10A-; -S-; -SO-; -SO2-;  $-s^+R^9A^-$ ;  $-PR^9$ -;  $-P^+R^9R^{10}A^-$ ;  $-P(O)R^9$ -; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have wherein  $\mathbb{R}^{16}$  and  $\mathbb{R}^{17}$  are independently selected from the group

consisting of R9 and M; and

R<sup>N</sup> is selected from the group consisting of hydrogen; alkyl; alkenyl; wherein M is a pharmaceutically acceptable cation; and wherein R, R, R, R, R, and A are as defined above; and

alkynyl; aralkyl; and heterocyclylalkyl; and

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120 heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy; -OR <sup>13</sup>; -NR <sup>13</sup>R <sup>14</sup>, -SR <sup>13</sup>, -S(O)R <sup>13</sup>; -S(O)R <sup>13</sup>; -SO<sub>3</sub>R <sup>13</sup>; -S<sup>+</sup>R <sup>13</sup>R <sup>14</sup>A; -NR <sup>13</sup>OR <sup>14</sup>; -NR <sup>13</sup>NR <sup>14</sup>R <sup>15</sup>; -CO<sub>2</sub>R <sup>13</sup>; -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>ONR <sup>13</sup>R <sup>14</sup>, -NR <sup>13</sup>CO<sup>2</sup>R <sup>13</sup>; -OM; -SO<sub>2</sub>CO<sup>2</sup>R <sup>13</sup> consisting of hydrogen; halogen; -CN; -NO2; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary one or more RX radicals are independently selected from the group

125 NR"C(O)R13, -C(O)NR13R14, -C(O)OM; -COR13, -OR18, -S(O)<sub>D</sub>NR13<sub>R</sub>14, -N<sub>R</sub>13<sub>R</sub>18, -N<sub>R</sub>18<sub>OR</sub>14, -N<sup>+</sup><sub>R</sub>13<sub>R</sub>14<sub>R</sub>15<sub>A</sub>; -<sub>PR</sub>13<sub>R</sub>14, -P(O)R 13R 14; -P+R 13R 14R 15A; amino acid residue; peptide residue; polypeptide residue; and carbohydrate residue;

135 130  $S^+R^0R^{10}A^-$ ; and carbohydrate residue; and CONR<sup>9</sup>R<sup>10</sup>; -SO<sub>2</sub>NR<sup>9</sup>R<sup>10</sup>; -PO(OR')OR''; -P<sup>9</sup>R<sup>10</sup>; -P<sup>+</sup>R<sup>9</sup>R<sup>11</sup>R<sup>12</sup>A; radicals selected from the group consisting of halogen; -CN; oxo; -OR 16, alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; NR9R10, -N+R9R10RWA; -SR16, -S(O)R9; -SO2R9; -SO3R16; -CO2R16, acyloxy radicals optionally may be further substituted with one or more wherein the R\* alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl

substituted with one or more radicals selected from the group consisting of halogen; -CN; -NO2; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl; wherein the R\* quaternary heterocyclyl radical optionally may be

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140 SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>, -C(O)NR<sup>13</sup>R<sup>14</sup>; -C(O)OM; -COR<sup>13</sup>; -P(O)R<sup>13</sup>R<sup>14</sup>, -P<sup>13</sup>R<sup>14</sup>; -P<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>-</sup>; -P(OR<sup>13</sup>)OR<sup>14</sup>; -S<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A<sup>-</sup>; - $N^{+}R^{13}R^{14}R^{15}A^{-}$ ; and carbohydrate residue; and heterocyclylalkyl; polyether; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO<sub>2</sub>R<sup>13</sup>; OM; -SO<sub>2</sub>OM; hydroxyalkyi; alkenyi; alkynyi; aryi; heterocyclyi; aryialkyi;

150 145 residue; polypeptide residue; carbohydrate residue; and polyalkyl optionally S<sup>+</sup>R<sup>13</sup>A<sup>-</sup>.; -PR<sup>13</sup>.; -P(O)R<sup>13</sup>.; -PR<sup>13</sup>R<sup>14</sup>, -P<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A<sup>-</sup>.; phenylene; amino wherein the R<sup>x</sup> radicals comprising carbon optionally may have one or more carbons replaced by -O-; -NR  $^{13}$ ; -N<sup>+</sup>R  $^{13}$ R  $^{14}$ A-; -S-; -SO-; -SO<sub>2</sub>; -SO-; -SO2-; -S<sup>†</sup>R<sup>9</sup>A-; -PR<sup>9</sup>-; -P<sup>†</sup>R<sup>9</sup>R<sup>10</sup>A-; or -P(O)R<sup>9</sup>-; and may have one or more carbons replaced by -O-; -NR 2; -N R R 10 A -; -S-; polyether; or polyalkyl; wherein said phenylene; amino acid residue; peptide acid residue; peptide residue; polypeptide residue; carbohydrate residue; wherein  $\mathbb{R}^{18}$  is selected from the group consisting of alkyl; alkenyl;

155 heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkoxycarbonyl; and

heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl radicals optionally may wherein the R1 alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary

50 ន be substituted with one or more radicals selected from the group consisting of defined above; or halogen; -CN; NO; oxo; -OR9; -NR9R10; -N+R9R11R12A; -SR9; -S(O)R<sup>9</sup>;-SO<sub>2</sub>R<sup>9</sup>;-SO<sub>3</sub>R<sup>9</sup>;-CO<sub>2</sub>R<sup>9</sup>;-CONR<sup>9</sup>R<sup>10</sup>;-SO<sub>2</sub>OM;-SO<sub>2</sub>NR<sup>9</sup>R<sup>10</sup>;-P(OR<sup>13</sup>)OR<sup>14</sup>;-PO(OR<sup>16</sup>)OR<sup>17</sup>; and -C(O)OM; and wherein R, R10, R11, R12, R13, R14, R15, R16, R17, R\*, A, and M are as

a pharmaceutically acceptable salt, solvate, or prodrug thereof

A compound of claim 1 wherein

q is an integer from 1 to 4;

hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; arylalkyl; alkoxyalkyl;  $\mathbb{R}^{1}$  and  $\mathbb{R}^{2}$  are independently selected from the group consisting of

alkoxyalkenyl; alkoxyalkynyl; alkylaryl; and (polyalkyl)aryl; or

 $R^1$  and  $R^2$  taken together with the carbon to which they are attached form  $C_3\text{-}C_{10}$  cycloalkenyl;

wherein the R<sup>1</sup> and R<sup>2</sup> alkyl; cycloalkyl; alkenyl; alkynyl; arylalkyl; alkoxyalkyl; alkoxyalkyl; alkoxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may be substituted with one or more radicals selected from the group consisting of -CN; halogen; oxo; -OR<sup>2</sup>; -NR<sup>2</sup>R<sup>10</sup>; -N<sup>4</sup>R<sup>9</sup>R<sup>10</sup>R<sup>W</sup>A<sup>2</sup>; -SR<sup>2</sup>; -S<sup>2</sup>R<sup>2</sup>; -SO<sub>2</sub>R<sup>2</sup>; -SO<sub>2</sub>R<sup>9</sup>; -CO<sub>2</sub>R<sup>9</sup>; and -CONR<sup>9</sup>R<sup>10</sup>; and

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wherein the R<sup>1</sup> and R<sup>2</sup> alkyl; cycloalkyl; alkenyl; alkynyl; arylalkyl;
15 alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; alkylaryl; and (polyalkyl)aryl
radicals optionally may have one or more carbons replaced by -O.; -NR<sup>9</sup>...
N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-., -S.; -SO.; -SO<sub>2</sub>.; -S<sup>+</sup>R<sup>9</sup>A-., -PR<sup>9</sup>.; -P(O)R<sup>9</sup>.; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-.,
or phenylene; and

wherein R<sup>9</sup>, R<sup>10</sup>, and R<sup>w</sup> are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; carboxyheterocyclyl; carboxyalkyl; carboxyheterocyclyl; carboxyalkyl; and acyl; and wherein A<sup>-</sup> is a pharmaceutically acceptable anion; and

R<sup>3</sup> and R<sup>4</sup> are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -SR<sup>9</sup>; S(O)R<sup>9</sup>; <sub>2</sub>SO<sub>2</sub>R<sup>9</sup>; and -SO<sub>3</sub>R<sup>9</sup>; or

 $R^3$  and  $R^4$  together form =0; =NOR?; =S; =NNR $^9$ R $^{10}$ ; =NR $^9$ ; or =CR $^{11}$ R $^{12}$ ;

wherein R<sup>11</sup> and R<sup>12</sup> are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; carboxyalkyl; cyanoalkyl; cyanoalkyl; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>9</sup>; -CO<sub>2</sub>R<sup>9</sup>; and -CONR<sup>9</sup>R<sup>10</sup>; or

 $R^{11}\,\mbox{and}\,R^{12}$  together with the carbon atom to which they are attached form a cyclic ring; and

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wherein R9 and R10 are as defined above; and

R<sup>5</sup> and R<sup>6</sup> are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; -OR<sup>9</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; and -SO<sub>3</sub>R<sup>9</sup>;

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wherein the R<sup>5</sup> and R<sup>6</sup> alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; and quaternary heterocyclyl radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; -CN; -NO2; oxo; alkyl; polyalkyl; haloalkyl; cycloalkyl; alkenyl; alkenyl; acyl; heterocyclyl; maternary heterocyclyl.

cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quatemary heterocyclyl;

45 arylalkyl; heterocyclylalkyl; polyether; -OR <sup>13</sup>; -NR <sup>13</sup>k <sup>14</sup>; -SC <sup>13</sup>; -SC)R <sup>13</sup>; -SO<sub>2</sub>R <sup>13</sup>; -NR <sup>13</sup>OR <sup>14</sup>; -NR <sup>13</sup>NR <sup>14</sup>R <sup>15</sup>; -CO<sub>2</sub>R <sup>13</sup>; -OM; 
SO<sub>2</sub>OM; -SO<sub>2</sub>NR <sup>13</sup>R <sup>14</sup>; -C(O)NR <sup>13</sup>R <sup>14</sup>; -C(O)M; -COC <sup>13</sup>; 
NR <sup>13</sup>C(O)R <sup>13</sup>; -NR <sup>13</sup>C(O)NR <sup>13</sup>R <sup>14</sup>; -C(O)NR <sup>13</sup>R <sup>14</sup>; -OC(O)NR <sup>13</sup>R <sup>14</sup>; -NR <sup>13</sup>COR <sup>13</sup>; -NR <sup>13</sup>COR <sup>13</sup>R <sup>14</sup>; -PR <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>13</sup>R <sup>14</sup>R <sup>1</sup>

N<sup>+</sup>R <sup>13</sup>R <sup>14</sup>R <sup>15</sup>A<sup>+</sup>; and wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclyllalkyl, and polyether substituents of the R<sup>2</sup> and R<sup>6</sup> radicals

the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclyl; arylalkyl; heterocyclyl; arylalkyl; heterocyclyl; -OR?; -NR?R<sup>8</sup>, -SR?; -S(O)R?; -SO2R?; -SO3R?; -CO2R?; -CO2R?; -N<sup>8</sup>, -N<sup>8</sup> R<sup>8</sup> R<sup>9</sup> A.; -PR?R<sup>8</sup>; -PR?R<sup>8</sup>; -PRR<sup>8</sup> R<sup>8</sup> R<sup>9</sup> A.; and -

60 P(O)(OR<sup>7</sup>)OR<sup>8</sup>; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R² and R² radicals optionally may have one or more carbons replaced by -O.; -NR<sup>7</sup>.; -N<sup>4</sup>R<sup>7</sup>R<sup>8</sup>A.; -S-; -SO-; -SO-; -SR<sup>7</sup>.; -P(O)R<sup>7</sup>.; -P<sup>4</sup>R<sup>7</sup>R<sup>8</sup>A.; or phenylene;

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wherein R<sup>7</sup> and R<sup>8</sup> are independently selected from the group consisting of hydrogen and alkyl; and

wherein R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclyl; quaternary heterocyclyl; alkylarylalkyl; alkylarylalkyl; alkylarmoniumalkyl; carboxyalkylamninocarbonylalkyl; and polyether or

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substituted with one or more radicals selected from the group consisting of are attached form a mono- or polycyclic heterocyclyl that is optionally oxo, carboxy, and quaternary salts; or wherein R13 and R14 together with the nitrogen atom to which they

are attached form a cyclic ring; and wherein  $\mathbb{R}^{14}$  and  $\mathbb{R}^{15}$  together with the nitrogen atom to which they

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alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; heterocyclylalkyi; quaternary heterocyclylalkyl; alkylarylalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; wherein the  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  alkyl; haloalkyl; cycloalkyl; polyalkyl;

8 radicals optionally may be substituted with one or more radicals selected from alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; the group consisting of halogen; -CN; sulfo; oxo; alkyl; sulfoalkyl;

S(0)R<sup>9</sup>; -S02R<sup>9</sup>; -S03R<sup>16</sup>; -C02R<sup>16</sup>; -CONR<sup>9</sup>R<sup>10</sup>; -S02NR<sup>9</sup>R<sup>10</sup>; -P(0)R<sup>16</sup>)OR<sup>17</sup>; -PR<sup>9</sup>R<sup>10</sup>; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>11</sup>A; -S<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A; and carboxyalkyl; guanidinyl; -OR16; -NR9R10; -N+R9R10RWA; -SR16; carbohydrate residue; and

alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; wherein the  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  alkyl; haloalkyl; cycloalkyl; polyalkyl;

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N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A·-; -S-; -SO-; -SO<sub>2</sub>-; -S<sup>+</sup>R<sup>9</sup>A·-; -PR<sup>9</sup>-; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A·-; -P(O)R<sup>9</sup>radicals optionally may have one or more carbons replaced by -O-; -NR2-; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl;

phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

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consisting of Ry and M; and wherein R<sup>16</sup> and R<sup>17</sup> are independently selected from the group

alkynyi; and aralkyi; and  $\mathbb{R}^{\mathbf{N}}$  is selected from the group consisting of hydrogen; alkyl; alkenyl; wherein R, R, R, R, R, R, and A are as defined above; and wherein M is a pharmaceutically acceptable cation; and

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consisting of hydrogen; halogen; -CN; -NO2; alkyl; cycloalkyl; polyalkyl one or more RX radicals are independently selected from the group

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15 110 arylalkyl; polyether; acyloxy; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -S<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -NR<sup>13</sup>OR<sup>14</sup>; <sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>-</sup>; -PR<sup>13</sup>R<sup>14</sup>; -P(O)R<sup>13</sup>R<sup>14</sup>; -P<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>-</sup>; amino acid C(O)OM; -COR13; -OR18; -S(O)nNR13R14; -NR13R18; -NR18OR14; -CO2R 13; -OM; -SO2OM; -SO2NR 13R 14; -NR "C(O)R"; -C(O)NR 13R 14, haloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl;

residue; peptide acid residue; polypeptide acid residue; and carbohydrate acid wherein the R\* alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl;

120 S<sup>+</sup>R<sup>9</sup>R <sup>10</sup>A ; and carbohydrate residue; and CONR 9R 10; -SO2NR 9R 10; -PO(OR 16)OR 17; -PR 9R 10; -P+R 9R 11R 12A; NR9R10,-N+R9R10RWA; -SR16; -S(O)R9; -SO2R9; -SO3R16; -CO2R16; and acyloxy radicals optionally may be further substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; -OR 10, alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether;

130 125 SO2NR 13R 14; -C(O)NR 13R 14; -C(O)OM; -COR 13; -P(O)R 13R 14; heterocyclylalkyl; polyether; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO<sub>2</sub>R<sup>13</sup>; OM; -SO<sub>2</sub>OM; - $N^{+}R^{13}R^{14}R^{15}A^{-}$ ; and carbohydrate residue; and PR 13R 14; P+R 13R 14R 15A; P(OR 13)OR 14; S+R 13R 14A; and hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; halogen; -CN; -NO2; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl; substituted with one or more radicals selected from the group consisting of wherein the R\* quaternary heterocyclyl radical optionally may be

40 135 wherein the RX radicals comprising carbon optionally may have one or more carbons replaced by -O-; -NR <sup>13</sup> -; -N<sup>+</sup>R <sup>13</sup>R <sup>14</sup>A-; -S-; -SO-; -SO<sub>2</sub>: -S<sup>+</sup>R <sup>13</sup>A<sup>-</sup>; -PR <sup>13</sup>; -PR <sup>13</sup>; -PR <sup>13</sup>A<sup>-</sup>A-; phenylene; amino N<sup>†</sup>R<sup>9</sup>R<sup>10</sup>A<sup>\*</sup>-; -S-; -SO-; -SO<sub>2</sub>-; -S<sup>†</sup>R<sup>9</sup>A-; -PR<sup>9</sup>-; -P<sup>†</sup>R<sup>9</sup>R<sup>10</sup>A-; or -P(O)R<sup>9</sup>optionally may have one or more carbons replaced by -O-; -NR'-; phenylene; amino acid; peptide; polypeptide; carbohydrate; and polyalkyl acid; peptide; polypeptide; carbohydrate; polyether; or polyalkyl; wherein said

alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; wherein  $\mathbb{R}^{18}$  is selected from the group consisting of alkyl; alkenyl;

145 heterocyclylalkoxycarbonyl; and

wherein the R<sup>11</sup> alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; -OR<sup>2</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N<sup>+</sup>R<sup>9</sup>R<sup>11</sup>R<sup>12</sup>A; -SR<sup>2</sup>S; -SO<sub>3</sub>R<sup>2</sup>; -CONR<sup>2</sup>R<sup>2</sup>DO(OR<sup>3</sup>S) - SO<sub>2</sub>OM; -SO<sub>2</sub>ONR<sup>2</sup>R<sup>10</sup>; - PR<sup>3</sup>R<sup>10</sup>; -P(OR<sup>3</sup>S)OR<sup>14</sup>; -PO(OR<sup>3</sup>S)OR<sup>17</sup>; and -C(O)OM; and

wherein R, R10, R11, R11, R14, R15, R16, R17, R1, A7, and M are as defined above; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof

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A compound of claim 1 wherein:

q is an integer from 1 to 4;

R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>2</sub>-C<sub>10</sub>)cycloalkyl; (C<sub>2</sub>-C<sub>10</sub>)alkynyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkyyl; (C<sub>1</sub>-C<sub>10</sub>)alkyyl; (C<sub>1</sub>-C<sub>10</sub>)alkyyl; (C<sub>1</sub>-C<sub>10</sub>)alkyyl; (C<sub>1</sub>-C<sub>10</sub>)alkyyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyyl; (C<sub>1</sub>-C<sub>10</sub>)alkyyl; aryl(aryl)aryl; ard (polyalky)laryl; or R<sup>1</sup> and R<sup>2</sup> taken together with the carbon to which they are attached

form (C<sub>2</sub>-C<sub>10</sub>)cycloalkyl; wherein the R<sup>1</sup> and R<sup>2</sup> (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl; (C<sub>3</sub>-

C<sub>10</sub>Jalkeny!; (C<sub>1</sub>-C<sub>10</sub>Jalkyny!; aryl(C<sub>1</sub>-C<sub>10</sub>Jalky)!; (C<sub>1</sub>-C<sub>10</sub>Jalkoxy(C<sub>1</sub>-C<sub>10</sub>Jalkyy);
 (C<sub>1</sub>-C<sub>10</sub>Jalkoxy(C<sub>2</sub>-C<sub>10</sub>Jalkeny!; (C<sub>1</sub>-C<sub>10</sub>Jalkoxy(C<sub>2</sub>-C<sub>10</sub>Jalkyny); (C<sub>1</sub>-C<sub>10</sub>Jalkylary!) and (polyalkyl)aryl radicals optionally may be substituted with one or more radicals selected from the group consisting of -CN; halogen; oxo; -OR 9: -NR<sup>2</sup>R<sup>10</sup>, -N<sup>2</sup>R<sup>2</sup>R<sup>10</sup>R wA; -SR<sup>3</sup>R<sup>10</sup>R wA; -SR<sup>3</sup>R<sup>10</sup>R wA; -SR<sup>3</sup>R wA; -PR<sup>3</sup>R<sup>10</sup>; p<sup>2</sup>R<sup>3</sup>R<sup>10</sup>R wA; -S(O)R<sup>3</sup>, -SO<sub>2</sub>R<sup>3</sup>; -SO<sub>3</sub>R<sup>3</sup>; -CO<sub>2</sub>R<sup>3</sup>; and -CONR<sup>3</sup>R<sup>10</sup>; and

15 P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>w</sup>A; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>9</sup>; -CO<sub>2</sub>R<sup>9</sup>; and -CONR<sup>9</sup>R<sup>10</sup>; an wherein the R<sup>1</sup> and R<sup>2</sup> (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl; (C<sub>2</sub>-C<sub>10</sub>)alkynyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>2</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkyly; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkyly; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>3</sub>-C<sub>10</sub>)alkynyl; (C<sub>1</sub>-C<sub>10</sub>)alkynyl; C<sub>10</sub>)alkylaryl; and (polyalkyl)aryl radicals optionally may have one or more carbons replaced by -O-; -NR<sup>2</sup>; -N<sup>+</sup>R<sup>3</sup>R<sup>10</sup>A-; -S-; -SO-; -SO<sub>2</sub>; -S<sup>+</sup>R<sup>3</sup>A-; -PR<sup>9</sup>; -P(O)R<sup>3</sup>; -P<sup>+</sup>R<sup>3</sup>R<sup>10</sup>A-; or phenylene; and

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wherein R<sup>9</sup>, R<sup>10</sup>, and R<sup>w</sup> are independently selected from the group consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-C<sub>10</sub>)eycloalkyl; (C<sub>3</sub>-C<sub>10</sub>)alkenyl; (C<sub>3</sub>-C<sub>10</sub>)alkynyl; aryl; heterocyclyl; ammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-

25 C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; carbo(C<sub>1</sub>-C<sub>10</sub>)alkylamino; and acyl; and carboxyheterocyclyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkylamino; and acyl; and

wherein A  $\bar{}$  is a pharmaceutically acceptable anion; and  $R^4$  are independently selected from the group consisting of

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hydrogen; (C,-C,<sub>10</sub>alkyl; (C<sub>7</sub>-C,<sub>10</sub>)alkenyl; (C<sub>7</sub>-C,<sub>10</sub>)alkynyl; aryl; heterocyclyl; OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO2R<sup>9</sup>; and -SO3R<sup>9</sup>; or R<sup>3</sup> and R<sup>4</sup> together form =0; =NOR<sup>9</sup>; =S; =NNR<sup>9</sup>R<sup>10</sup>; =NR<sup>9</sup>; or =CR<sup>11</sup>R<sup>12</sup>;

wherein R<sup>11</sup> and R<sup>12</sup> are independently selected from the group
consisting of hydrogen; -CN; halogen; oxo; (C<sub>1</sub>-C<sub>10</sub>alkyl; (C<sub>2</sub>-C<sub>10</sub>alkyl;
(C<sub>2</sub>-C<sub>10</sub>alkynyl; aryl; heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>alkyl;
carbox(C<sub>1</sub>-C<sub>10</sub>alkoxy(C<sub>1</sub>-C<sub>10</sub>alkyl; (C<sub>3</sub>-C<sub>10</sub>cycloalkyl; cyano(C<sub>1</sub>-C<sub>10</sub>alkyl;
OR<sup>2</sup>; -NR<sup>2</sup>R<sup>10</sup>; -SR<sup>2</sup>; -S(O)R<sup>2</sup>; -SO<sub>2</sub>R<sup>2</sup>; -SO<sub>3</sub>R<sup>2</sup>; -CO<sub>2</sub>R<sup>2</sup>; and

CONR<sup>9</sup>R <sup>10</sup>, or
All and R <sup>12</sup> together with the carbon atom to which they are attached form a cyclic ring; and

wherein R9 and R10 are as defined above; and

R<sup>5</sup> and R<sup>6</sup> are independently selected from the group consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl; (C<sub>3</sub>-C<sub>10</sub>)alkenyl; (C<sub>4</sub>-C<sub>10</sub>)alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; -OR<sup>9</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO2R<sup>9</sup>;

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and -SO<sub>3</sub>R<sup>9</sup>;
wherein the R<sup>5</sup> and R<sup>6</sup> (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl; (C<sub>3</sub>-C<sub>10</sub>)alkenyl; (C<sub>3</sub>-C<sub>10</sub>)alkenyl; and quaternary heterocyclyl and quaternary heterocyclyl radicals optionally may be substituted with one or more radicals independently

55 SO<sub>2</sub>OM; -SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>; -C(O)NR<sup>13</sup>R<sup>14</sup>; -C(O)OM; -COR<sup>13</sup>; -NR<sup>12</sup>(O)R<sup>1</sup>; -NR<sup>13</sup>C(O)NR<sup>18</sup>R<sup>13</sup>; -NR<sup>13</sup>CO<sub>2</sub>R<sup>14</sup>; -OC(O)NR<sup>13</sup>R<sup>14</sup>;

- S 8  $P(O)R^7R^8$ ;  $-PR^7R^8$ ;  $-P^+R^7R^8R^9A^-$ ; and  $-P(O)(OR^7)OR^8$ ; and S(O)R'; -SO2R'; -SO3R'; -CO2R'; -CONR'R8; -N+R'R8R9A; heterocyclyl(C1-C10)alkyl; quaternary heterocyclyl; -OR7; -NR7R8; -SR7; -(C2-C10)alkenyl; (C2-C10)alkynyl; aryl; heterocyclyl; aryl(C1-C10)alkyl; consisting of -CN; halogen; hydroxy; oxo; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl; be further substituted with one or more radicals selected from the group C<sub>10</sub>)alkyl, and polyether substituents of the R<sup>3</sup> and R<sup>6</sup> radicals optionally may heterocyclyl, quaternary heterocyclyl, aryl(C1-C10)alkyl, heterocyclyl(C1- $C_{10}$ ) alkyl,  $(C_3-C_{10})$  cycloalkyl,  $(C_2-C_{10})$  alkenyl,  $(C_2-C_{10})$  alkynyl, aryl, wherein the (C<sub>1</sub>-C<sub>10</sub>)alkyl, polyalkyl, halo(C<sub>1</sub>-C<sub>10</sub>)alkyl, hydroxy(C<sub>1</sub>-
- SO2-; -STR'A-; -PR'-; -P(O)R'-; -PTR'R'A-; or phenylene; and  $C_{10}$ )alkyl,  $(C_3$ - $C_{10}$ )cycloalkyl,  $(C_3$ - $C_{10}$ )alkenyl,  $(C_7$ - $C_{10}$ )alkynyl, aryl, have one or more carbons replaced by -O-; -NR '-; -NTR 'R 'A-; -S-; -SO-; -C<sub>10</sub>)alkyl, and polyether substituents of the R' and R' radicals optionally may heterocyclyl, quaternary heterocyclyl, aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl, heterocyclyl(C<sub>1</sub>wherein the (C<sub>1</sub>-C<sub>10</sub>)alkyl, polyalkyl, halo(C<sub>1</sub>-C<sub>10</sub>)alkyl, hydroxy(C<sub>1</sub>-

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consisting of hydrogen and (C1-C10)alkyl; and wherein  $R^{\overline{I}}$  and  $R^{\overline{B}}$  are independently selected from the group

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polyalkyl; (C2-C10)alkenyl; (C2-C10)alkynyl; aryl; heterocyclyl; quaternary carboxy(C<sub>1</sub>-C<sub>10</sub>)alkylaminocarbonyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether; or C<sub>10</sub>)alkylheterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylaryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl; heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary wherein  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  are independently selected from the group

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substituted with one or more radicals selected from the group consisting of are attached form a mono- or polycyclic heterocyclyl that is optionally oxo, carboxy, and quaternary salts; or wherein R13 and R14 together with the nitrogen atom to which they

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are attached form a cyclic ring; and wherein R 14 and R 15 together with the nitrogen atom to which they

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carboxy(C<sub>1</sub>-C<sub>10</sub>)alkylaminocarbonyl (C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether radicals  $C_{10}$ ) alky lheterocycly  $(C_1 - C_{10})$  alky  $(C_1 - C_{10})$  alky lammonium  $(C_1 - C_{10})$  alky  $(C_1 - C_{10})$ C10)cycloalkyi; polyalkyi; (C2-C10)alkenyi; (C2-C10)alkynyi; aryi; heterocyclyi optionally may be substituted with one or more radicals selected from the aminocarbonyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylaminocarbonyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary heterocyclyl( $C_i$ - $C_{i0}$ )alkyl; ( $C_i$ - $C_{i0}$ )alkylaryl ( $C_i$ - $C_{i0}$ )alkyl; ( $C_i$ quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; wherein the  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-

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ខ C<sub>in</sub>)alkyl; carboxy; carboxy(C<sub>1</sub>-C<sub>in</sub>)alkyl; guanidinyl; -OR<sup>16</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>W</sup>A<sup>-</sup>; -SR<sup>16</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>16</sup>; -CO<sub>2</sub>R<sup>16</sup>; -CONR<sup>9</sup>R<sup>10</sup>; -- SO<sub>2</sub>NR<sup>9</sup>R<sup>10</sup>; -PO(OR<sup>16</sup>)OR<sup>17</sup>; -PR<sup>9</sup>R<sup>10</sup>; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>11</sup>A C10) alkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl(C1--S<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-; and carbohydrate residue; and

group consisting of halogen; -CN; sulfo; oxo; (C<sub>1</sub>-C<sub>10</sub>)alkyl; sulfo(C<sub>1</sub>-

115 <del>1</del>0 505 polypeptide residue; and NTRYR10A-; -S-; -SO-; -SO<sub>2</sub>-; -S<sup>†</sup>R<sup>9</sup>A-; -PR<sup>9</sup>-; -P<sup>†</sup>R<sup>9</sup>R<sup>10</sup>A-; -P(O)R<sup>9</sup>-; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkylaminocarbonyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether radicals aminocarbonyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylaminocarbonyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; optionally may have one or more carbons replaced by -O-; -NR9-; phenylene; carbohydrate residue; amino acid residue; peptide residue; or C<sub>10</sub>)alkylheterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylaryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl;  $C_{10}$ )cycloalkyl; polyalkyl; ( $C_2$ - $C_{10}$ )alkenyl; ( $C_2$ - $C_{10}$ )alkynyl; aryl; heterocyclyl; wherein the R  $^{13}$ , R  $^{14}$ , and R  $^{15}$  (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>-

consisting of R7 and M; and wherein  $\mathbb{R}^{16}$  and  $\mathbb{R}^{17}$  are independently selected from the group

(C<sub>2</sub>-C<sub>10</sub>)alkenyl; (C<sub>2</sub>-C<sub>10</sub>)alkynyl; and aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; and  $\mathbb{R}^{N}$  is selected from the group consisting of hydrogen;  $(C_{i}\text{-}C_{i0})$ alkyl; wherein R, R, R, R, R, R, and A are as defined above; and wherein M is a pharmaceutically acceptable cation; and

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aryl; heterocyclyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; polyether; consisting of hydrogen; halogen; -CN; -NO2; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>3</sub>- $C_{10}$ )cycloalkyl; polyalkyl; halo $(C_1-C_{10})$ alkyl;  $(C_2-C_{10})$ alkenyl;  $(C_2-C_{10})$ alkynyl; one or more RX radicals are independently selected from the group

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acyloxy; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -S(O)2R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -O<sub>2</sub>R<sup>13</sup>; -O<sub>2</sub>R<sup>13</sup>; -O<sub>3</sub>; -O<sub>4</sub>; -O<sub>5</sub>R<sup>13</sup>; -O<sub>6</sub>; -O<sub>6</sub>; -O<sub>7</sub>; 
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wherein the R¹ (C₁-C₁₀)alkyl; (C₁-C₁₀)cycloalkyl; polyalkyl; halo(C₁-C₁₀)alkyl; hydroxy(C₁-C₁₀)alkyl; (C₁-C₁₀)alkenyl; (C₁-C₁₀)alkynyl; aryl; heterocyclyl; aryl(C₁-C₁₀)alkyl; heterocyclyl(C₁-C₁₀)alkyl; polyether; and acyloxy radicals optionally may be further substituted with halogen; -CN; oxo; -OR¹6; -NRŶR¹0; -N⁴ŶR¹1R²A⁻; -SR¹6; -S(O)R³; -SO2R³; -SO3R¹6; -CO2R¹6; -CONRŶR¹0; -S^2R³\*0, -P\P\$R¹1R²A⁻; or -S⁴R²ŶR¹0, -PO(OR¹⁰)OR¹¹; -PRŶR¹0; -PRŶR¹1R²A⁻; or -S⁴R²ŶR¹0, -And

wherein the R\* quatemary heterocyclyl radical optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; -NO2; oxo; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>2</sub>-C<sub>10</sub>)cycloalkyl; polyalkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; hydroxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>2</sub>-C<sub>10</sub>)alkyl; polyalkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; polyalkyl; aryl; heterocyclyl; -SO<sub>1</sub> 13; -SO<sub>2</sub> 13; -SO<sub>2</sub> 13; -SO<sub>2</sub> 14; -SO<sub>1</sub> 14; -SO<sub>1</sub> 14; -SO<sub>2</sub> 14; -SO<sub>2</sub> 15; -SO<sub>2</sub> 16; -SO<sub>2</sub> 16; -SO<sub>2</sub> 17; -SO<sub>2</sub> 16; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -SO<sub>2</sub> 17; -S

wherein the R<sup>x</sup> radicals comprising carbon optionally may have one or more carbons replaced by -O.; -NR<sup>13</sup>; -N<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A·; -S·; -SO.; -SO.; -SO.; -SO.; -SO.; -SO.; -P. S<sup>+</sup>R<sup>13</sup>A<sup>-</sup>; -PR<sup>13</sup>; -P(O)R<sup>13</sup>; -PR<sup>13</sup>; -P<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A·; phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; polyether; or polyalkyl; wherein said phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; and polyalkyl optionally may have one or more carbons replaced by -O.; -NR<sup>9</sup>; -N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A·; -S·; -SO.; -SO.; -S<sup>+</sup>R<sup>9</sup>A·; -PR<sup>9</sup>; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A·; or -P(O)R<sup>9</sup>; and

wherein R<sup>18</sup> is selected from the group consisting of (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; acyl; and aryl(C<sub>1</sub>-C<sub>10</sub>)alkoxycarbonyl; and

wherein the R<sup>11</sup> (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary heterocyclyl; 160 aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; acyl; and aryl(C<sub>1</sub>-C<sub>10</sub>)alkoxycarbonyl radicals optionally

may be substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; -OR $^2$ ; -NR $^2$ R $^1$ 0; -N^+R $^2$ R $^1$ 1R $^1$ A; -SR $^2$ ; -S(O)R $^2$ ; -SO2R $^3$ ; -CO2R $^3$ ; -CONR $^3$ R $^1$ 0; -SO2OM; -SO2NR $^3$ R $^1$ 0; -P(OR $^1$ 3)OR $^1$ 4; -PO(OR $^1$ 5)OR $^1$ 7; and -C(O)OM; and

165 wherein R\*, R", R", R", R", R", R", R", R", R", A", and M are as defined above; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof; and provided that aryl is selected from the group consisting of optionally substituted phenyl, biphenyl and naphthyl; and

provided that heterocyclyl is selected from the group consisting of optionally substituted heterocyclyl comprising a 5 to 10 membered ring and comprising one or more ring atoms that are heteroatoms selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus.

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5. A compound of claim 1 wherein:

q is an integer from 1 to 4;

R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, pentyl, hexyl, phenoxymethylene, phenoxyethylene, phenoxypropylene, pyridinyloxymethylene, pyridinyloxymethylene, pyridinyloxyethylene, pyrimidinyloxymethylene, methylpyridinyloxyethylene, pyrimidinyloxyethylene, or

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 $R^1 \ {\rm and} \ R^2$  taken together with the carbon to which they are attached form cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl; and

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R<sup>3</sup> and R<sup>4</sup> are independently selected from the group consisting of hydrogen, hydroxy, methyl, ethyl, phenyl, pyridinyl, amino, methylamino, dimethylamino, ethylamino and diethylamino; and

R<sup>2</sup> and R<sup>4</sup> are independently selected from the group consisting of hydrogen, phenyl, chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, hydroxyphenyl, methoxyphenyl, methoxyphenyl, methoxyforomophenyl), methoxyforomophenyl), methoxyforomophenyl), ethoxyforomophenyl), ethoxyforomophenyl), ethoxyforomophenyl), ethoxyforomophenyl), ethoxyforomophenyl, arminophenyl, methylaminophenyl, dimethylaminophenyl, dimethylaminophenyl, diethylaminophenyl,

trimethylammoniumphenyl, triethylammoniumphenyl,

23 trimethylammoniumbutylcarbonylaminophenyl, triethylammoniumpropylcarbonylaminophenyl, triethylammoniumethylcarbonylaminophenyl, triethylammoniummethylcarbonylaminophenyl, trimethylammoniummethylcarbonylaminophenyl triethylammoniumbutylcarbonylaminophenyl, methylcarbonylaminophenyl trimethylammoniumpropylcarbonylaminophenyl, trimethylammoniumethylcarbonylaminophenyl,

ဗ 엉 ethylcarbonylaminophenyl, chloroethylcarbonylaminophenyl, chloromethylcarbonylaminophenyl, fluoromethylcarbonylaminophenyl, bromomethylcarbonylaminophenyl, iodomethylcarbonylaminophenyl, iodoethylcarbonylaminophenyl, propylcarbonylaminophenyl, fluoroethylcarbonylaminophenyl, bromoethylcarbonylaminophenyl,

8 methylpyridinyl, pyridinium, methylpyridinium, thienyl, chlorothienyl, chloropropylcarbonylaminophenyl, fluoropropylcarbonylaminophenyl, butylcarbonylaminophenyl, chlorobutylcarbonylaminophenyl, bromopropylcarbonylaminophenyl, iodopropylcarbonylaminophenyl, fluorothienyl, bromothienyl, iodothienyl; methoxycarbonylphenyl, iodobutylcarbonylaminophenyl, 3,4-dioxymethylenephenyl, pyridinyl, fluorobutylcarbonylaminophenyl, bromobutylcarbonylaminophenyl,

ટ piperazinyloxymethoxyethoxyethoxyphenyl, pyridiniumethoxyethoxyethoxyphenyl, bromoethoxyethoxyethoxyphenyl, iodoethoxyethoxyethoxyphenyl chloroethoxyethoxyethoxyphenyl, fluoroethoxyethoxyethoxyphenyl triethylammoniumethoxyethoxyethoxyphenyl,

ethoxycarbonylphenyl, trimethylammoniumethoxyethoxyethoxyphenyl

dimethylpiperidinyloxymethoxyethoxyethoxyphenyl; and methylpiperidinyloxymethoxyethoxyethoxyphenyl, and piperidinyloxymethoxyethoxyethoxyphenyl, dimethylpiperazinyloxymethoxyethoxyethoxyphenyl,

methylpiperazinyloxymethoxyethoxyethoxyphenyl,

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propyl, n-butyl, n-pentyl, n-hexyl and benzyl; and RN is selected from the group consisting of hydrogen, methyl, ethyl, n-

consisting of hydroxy, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl one or more Rx radicals are independently selected from the group

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methylsulfinyl, methylsulfonyl, ethylthio, ethylsulfinyl, ethylsulfonyl, amino, tert-butyl, sec-butyl, methoxy, ethoxy, n-propoxy, isopropoxy, methylthio, hydroxyamino, methylamino, dimethylamino, ethylamino, diethylamino,

S 8 hexylcarbonylamino, benzyloxycarbonylamino, aminoimidocarbonylamino, trimethylammonium, triethylammonium, N-methyl-N-carboxymethyl-amino, n-propylcarbonylamino, n-butylcarbonylamino, n-pentylcarbonylamino, nbromomethylcarbonylamino, iodomethylcarbonylamino, ethylcarbonylamino chloromethylcarbonylamino, fluoromethylcarbonylamino, N,N-dimethyl-N-carboxymethyl-ammonium, methylcarbonylamino,

70 pyrrolidine, N-methyl-pyrrolidinium, piperazinyl, N-methylpiperazinyl, N,N' pipendinium, and thienyl; or dimethyl-piperazinium, piperidinyl, methylpiperidinyl, N-methylmorpholinyl, N-methyl-morpholinium, azetidinyl, N-methyl-azetidinium,

a pharmaceutically acceptable sait, solvate, or prodrug thereof.

A compound of claim 1 wherein:

q is an integer from 1 to 4;

hydrogen and (C<sub>1</sub>-C<sub>10</sub>)alkyl; or  $\mathbb{R}^{1}$  and  $\mathbb{R}^{2}$  are independently selected from the group consisting of

form (C3-C10)cycloalkyl; and R1 and R2 taken together with the carbon to which they are attached

hydrogen and hydroxy; and  $\mathbb{R}^3$  and  $\mathbb{R}^4$  are independently selected from the group consisting of

5 more radicals independently selected from the group consisting of halogen; hydroxy; -NO2; (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; polyether; -OR  $^{13}$ ; -NR  $^{13}$ R  $^{14}$ ; and -NR  $^{13}$ C(O)R  $^{14}$ . R2 is phenyl, wherein said phenyl is optionally substituted with one or

(C<sub>1</sub>-C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether; or consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary heterocyclyl( $C_1$ - $C_{10}$ )alkyl; ( $C_1$ - $C_{10}$ )alkylheterocyclyl( $C_1$ - $C_{10}$ )alkyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; wherein  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$  and  $\mathbb{R}^{15}$  are independently selected from the group

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20 heterocyclyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub> wherein the R  $^{13}$ , R  $^{14}$ , and R  $^{15}$  (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl;

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C<sub>10</sub>Jalkyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>Jalkyl; (C<sub>1</sub>-C<sub>10</sub>Jalkylheterocyclyl(C<sub>1</sub>-C<sub>10</sub>Jalkyl; (C<sub>1</sub>-C<sub>10</sub>Jalkyltammonium(C<sub>1</sub>-C<sub>10</sub>Jalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; (C<sub>1</sub>-C<sub>10</sub>Jalkyl; heterocyclyl; quaternary

- 25 heterocyclyi; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; -OR<sup>16</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N<sup>4</sup>R<sup>9</sup>R<sup>10</sup>R<sup>W</sup>A; and -CONR<sup>9</sup>R<sup>10</sup>; and wherein R<sup>9</sup> and R<sup>10</sup> are independently selected from the group consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; ammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl;
  - 30 C<sub>10</sub>Jalkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>Jalkyl; carbo(C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>1</sub>-C<sub>10</sub>Jalkyl; carboxyheterocyclyl; carboxy(C<sub>1</sub>-C<sub>10</sub>Jalkylamino; and acyj; and wherein A<sup>-</sup> is a pharmaceutically acceptable anion; and wherein R<sup>11</sup> and R<sup>12</sup> are independently selected from the group
- consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl;

  carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; and carbo(C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; or

  R<sup>11</sup> and R<sup>12</sup> together with the carbon atom to which they are attached form a cyclic ring; and
- wherein R" and R16 are as defined in claim 2; and
  R6 is hydrogen; and
  RN is selected from the group consisting of hydrogen; (C,-C,0)alky);
  and aryl(C,-C,0)alky); and
  - one or more R<sup>x</sup> radicals are independently selected from the group consisting of hydrogen; -NO<sub>2</sub>; (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>;
- wherein R<sup>13</sup> and R<sup>14</sup> are as defined above; or a pharmaceutically acceptable salt, solvate, or prodrug thereof; and provided that aryl is selected from the group consisting of optionally substituted phenyl, biphenyl and naphthyl; and

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- provided that heterocyclyl is selected from the group consisting of optionally substituted heterocyclyl comprising a 5 to 10 membered ring and comprising one or more ring atoms that are heteroatoms selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus.
- 7. A compound of claim 1 wherein:
- q is an integer from 1 to 4;

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 $R^{1}\,\mbox{and}\,\,R^{2}$  are independently selected from the group consisting of ethyl and n-butyl; or

 ${\bf R}^1$  and  ${\bf R}^2$  taken together with the carbon to which they are attached form eyclopenty!, and

60 . one of R<sup>3</sup> and R<sup>4</sup> is hydrogen and the other of R<sup>3</sup> and R<sup>4</sup> is hydroxy; and

 ${\bf R}^{S}$  is selected from the group consisting of phenyl, hydroxyphenyl, methoxyphenyl, nitrophenyl, aminophenyl, methylaminophenyl, dimethylaminophenyl, ethylaminophenyl,

- 65 diethylaminophenyl, trimethylammoniumphenyl, triethylammoniumphenyl, trimethylammoniummethylcarbonylaminophenyl, triethylammoniummethylcarbonylaminophenyl, trimethylammoniumethylcarbonylaminophenyl,
- 70 trimethylammoniumpropylcarbonylaminophenyl, triethylammoniumpropylcarbonylaminophenyl, trimethylammoniumbutylcarbonylaminophenyl, triethylammoniumbutylcarbonylaminophenyl, methylcarbonylaminophenyl,

riethylammoniumethylcarbonylaminophenyl,

- chloromethylcarbonylaminophenyl, fluoromethylcarbonylaminophenyl, bromomethylcarbonylaminophenyl, iodomethylcarbonylaminophenyl, ethylcarbonylaminophenyl, ethylcarbonylaminophenyl, fluoroethylcarbonylaminophenyl, bromoethylcarbonylaminophenyl, iodoethylcarbonylaminophenyl, propylcarbonylaminophenyl, chloropropylcarbonylaminophenyl, chloropropylcarbonylaminophenyl,
  - 80 bromopropylcarbonylaminophenyl, iodopropylcarbonylaminophenyl, butylcarbonylaminophenyl, chlorobutylcarbonylaminophenyl, fluorobutylcarbonylaminophenyl, bromobutylcarbonylaminophenyl, bromobutylcarbonylaminophenyl, iodobutylcarbonylaminophenyl,
- trimethylarumoniumethoxyethoxyethoxyphenyl, 85 triethylarumoniumethoxyethoxyethoxyphenyl,
- chloroethoxyethoxyphenyl, fluoroethoxyethoxyphenyl, bromoethoxyethoxyphenyl, iodoethoxyethoxyphenyl, and pyridiniumethoxyethoxyphenyl; and

R6 is hydrogen;

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 $\mathbf{R}^{\mathbf{N}}$  is selected from the group consisting of hydrogen, methyl, ethyl, and benzyl; and

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one or more R<sup>X</sup> radicals are independently selected from the group consisting of hydroxy, methyl, ethyl, methoxy, ethoxy, amino, hydroxyamino, methylamino, dimethylamino, ethylamino, diethylamino,

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trimethylammonium, triethylammonium, N-methyl-N-carboxymethyl-amino, N,N-dimethyl-N-carboxymethyl-ammonium, methylcarbonylamino, chloromethylcarbonylamino, fluoromethylcarbonylamino, bromomethylcarbonylamino, iodomethylcarbonylamino, ethylcarbonylamino, benzyloxycarbonylamino, and aminoimidocarbonylamino; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

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 A compound of claim 1 selected from the compounds of the group consisting of:

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4R,5R)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

5-chloro-N-[3-[(4K,SR)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]pentanamide;

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5-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-N,N,N-triethyl-5-oxo-pentanaminium trifluoroacetate;

2-chloro-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-y]phenyl]acetamide;

2-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino]-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-N,N,N-triethyl-2-oxoethanaminium chloride;

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(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4R,SR)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-(((2-iodoethyoxy)ethoxy)ethoxy)phenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

1-[2-[2-[4-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]ethyl]pyridinium;

2-[2-[4-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]-N,N,N-triethylethanaminium iodide;

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide and (4S,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4R,5R)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-1,2-benzothiazepin-4-ol 1,1-dioxide;

5-bromo-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl)phenyl]pentanamide;

5-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-N,N,N-triethyl-5-oxo-1-pentanaminium trifluoroacetate;

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-phenyl-1,2benzothiazzpin-4-ol 1,1-dioxide;

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

2-[2-[2-[4-[(4R,5R)-3,3-dibutyl-7- (dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]-N,N,N-triethylethanaminium iodide;

(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-2. (phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4R,SR)-3,3-dibutyl-7-(dimethylamino)-5-[3-(ethylamino)phenyl]-2,3,4,5tetrahydro-2- (phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide; (4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide; and

(4R,5R)-7-dimethylamino)-2-ethyl-4,5-dihydro-5-(4-methoxyphenyl)-spiro[1,2-benzothiazepine-3(2H),1'-cyclopentan]-4-ol 1,1-dioxide; and

their pharmaceutically acceptable salts.

9. A compound of claim 2 wherein  $\mathbb{R}^5$  and  $\mathbb{R}^6$  are independently selected from the group consisting of H; aryl; heterocyclyl; and quaternary heterocyclyl;

wherein the R<sup>5</sup> and R<sup>6</sup> aryl; heterocyclyl; and quatemary heterocyclyl radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; -CN; -NO2; oxo; alkyl; polyalkyl; haloalkyl; haloakyl; alkenyl; alkynyl; aryl; heterocyclyl; quatemary heterocyclyl; arylalkyl; heterocyclyl; golyether,

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OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; 
NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO<sub>2</sub>R<sup>13</sup>; -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>; -C(O)NR<sup>13</sup>R<sup>14</sup>; -C(O)OM; -COR<sup>13</sup>; -NR<sup>13</sup>C(O)R<sup>1</sup>; -NR<sup>13</sup>C(O)R<sup>1</sup>; -NR<sup>13</sup>CO)R<sup>1</sup>; -NR<sup>13</sup>CO)R<sup>1</sup>; -NR<sup>13</sup>CO)R<sup>1</sup>; -NR<sup>13</sup>CO)R<sup>1</sup>; -NR<sup>13</sup>CO)R<sup>1</sup>; -NR<sup>13</sup>CO)R<sup>1</sup>; -NR<sup>13</sup>CO)R<sup>13</sup>F<sup>14</sup>; -P(O)R<sup>13</sup>F<sup>14</sup>; -P(O)R<sup>13</sup>F<sup>14</sup>; -P(O)R<sup>13</sup>F<sup>14</sup>; -P(O)R<sup>13</sup>F<sup>14</sup>; -P(O)R<sup>13</sup>F<sup>14</sup>; -P(O)R<sup>13</sup>F<sup>14</sup>; -R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>; -R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>14</sup>R<sup>13</sup>F<sup>1</sup>

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclyl quaternary heterocyclylalkyl, and polyether substituents of the R³ and R6 radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy, oxo; alkyl; cycloalkyl; alkenyl;

20 alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; -OR<sup>7</sup>; -NR<sup>7</sup>R<sup>8</sup>; -SR<sup>7</sup>; -S(O)R<sup>7</sup>; -SO2R<sup>7</sup>; -SO3R<sup>7</sup>; -CO3R<sup>7</sup>; -CONR<sup>7</sup>R<sup>8</sup>; -N<sup>4</sup>R<sup>7</sup>R<sup>8</sup>R<sup>9</sup>A; -P(O)R<sup>7</sup>R<sup>8</sup>; -P<sup>4</sup>R<sup>7</sup>R<sup>8</sup>P<sup>9</sup>A; and P(O)(OR<sup>7</sup>)OR<sup>8</sup>; and

wherein the alkyi, polyalkyi, haloalkyi, hydroxyalkyi, cycloalkyi, alkenyi, alkynyi, aryi, heterocyclyi, quatemary heterocyclyi, aryialkyi, heterocyclylalkyi, and polyether substituents of the R² and R⁴ radicals optionally may have one or more carbons replaced by -O.; -NR<sup>7</sup>; -N<sup>4</sup>R<sup>7</sup>R<sup>8</sup>A·; -S·; -SO; -SO; -S<sup>4</sup>R<sup>7</sup>A·; -P(O)R<sup>7</sup>; -P<sup>4</sup>R<sup>7</sup>R<sup>8</sup>A·; or phenylene; and

wherein R<sup>7</sup> and R<sup>8</sup> are independently selected from the group consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and wherein R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl;

alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl;
heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl;
alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl;
alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R<sup>13</sup> and R<sup>14</sup> together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy,

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and quaternary salts; or wherein  $R^{15}$  together with the nitrogen atom to which they are attached form a cyclic ring; and

alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; wherein the R  $^{13}$  , R  $^{14}$  , and R  $^{15}$  alkyl; haloalkyl; cycloalkyl; polyalkyl;

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S -OR<sup>16</sup>, NR<sup>9</sup>R<sup>10</sup>, N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>W</sup>A<sup>-</sup>; -SR<sup>16</sup>, -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>16</sup>, -CO<sub>2</sub>R<sup>16</sup>, -CONR<sup>9</sup>R<sup>10</sup>, -SO<sub>2</sub>NR<sup>9</sup>R<sup>10</sup>, -PO(OR<sup>16</sup>)OR<sup>17</sup>, -PR<sup>9</sup>R<sup>10</sup>, -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>11</sup>A<sup>-</sup>; -S<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A<sup>-</sup>; and carbohydrate residue; and the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary

radicals optionally may be substituted with one or more radicals selected from

S wherein the  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  alkyl; haloalkyl; cycloalkyl; polyalkyl;

alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl;

alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl;

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N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-; -S-; -SO-; -SO<sub>2</sub>-; -S<sup>+</sup>R<sup>9</sup>A-; -PR<sup>9</sup>-; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-; -P(O)R<sup>9</sup>-; radicals optionally may have one or more carbons replaced by -O-; -NR2-; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether phenylene; carbohydrate residue; amino acid residue; peptide residue; or

consisting of R and M; and polypeptide residue; and wherein  $\mathbb{R}^{16}$  and  $\mathbb{R}^{17}$  are independently selected from the group

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wherein R9, R10, R11, R12, Rw, and A are as defined in claim 2. wherein M is a pharmaceutically acceptable cation; and

5 A compound of claim 2 wherein R<sup>5</sup> or R<sup>6</sup> has the formula

#### -Ar-(R<sup>y</sup>),

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t is an integer from 0 to 5;

piperazinyl; piperonyl; pyrrolyl; naphthyl; furanyl; anthracenyl; quinolinyl; isoquinolinyl; quinoxalinyl; imidazolyl; pyrazolyl; oxazolyl; isoxazolyl; Ar is selected from the group consisting of phenyl; thiophenyl; pyridyl

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5 pyrimidinyl; thiazolyl; triazolyl; isothiazolyl; indolyl; benzoimidazolyl; benzoxazolyl; benzothiazolyl; and benzoisothiazolyl; and one or more  $\mathbb{R}^{\mathbf{y}}$  are independently selected from the group consisting of

5 cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; -OR <sup>13</sup>; -NR <sup>13</sup>R <sup>14</sup>, -SR <sup>13</sup>; -SO<sub>3</sub>R <sup>13</sup>; -NR <sup>13</sup>OR <sup>14</sup>; -NR <sup>13</sup>NR <sup>14</sup>R <sup>15</sup>; -CO<sub>2</sub>R <sup>13</sup>; -OM; -NR13C(0)R14; -NR13C(0)NR14R15; -NR13CO,R15; -OC(0)R13; -OC(0)NR13R15; SO20M; -SO2NR 13R 14; -C(O)NR 13R 14; -C(O)OM; -COR 13; halogen; -CN; -NO2; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl;

20 -NR''SOR''; -NR''SO,R''; -NR''SONR''R'; -NR''SO,NR''R'; -P(O)R'13R'14, -PR'13R'14, -P'R'13R'14R'15A'; -P(OR'13)OR'14, -S'R'13R'14A'; and -N+R13R14R15A; and

ä 23 aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; -OR' be further substituted with one or more radicals selected from the group N<sup>†</sup>R<sup>7</sup>R<sup>8</sup>R<sup>9</sup>A-; -P(O)R<sup>7</sup>R<sup>8</sup>; -PR<sup>7</sup>R<sup>8</sup>; -P<sup>†</sup>R<sup>7</sup>R<sup>8</sup>R<sup>9</sup>A<sup>-</sup>; and -P(O)(OR<sup>7</sup>)OR<sup>8</sup>; -NR 7R 8; -SR 7; -S(O)R 7; -SO2R 7; -SO3R 7; - CO2R 7; -CONR 7R 5; consisting of -CN, halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; heterocyclylalkyl, and polyether substituents of the RY radicals optionally may alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl,

SO2-; -S<sup>†</sup>R<sup>7</sup>A-; -PR<sup>7</sup>-; -P(O)R<sup>7</sup>-; -P<sup>†</sup>R<sup>7</sup>R<sup>8</sup>A-; or phenylene; and have one or more carbons replaced by .O.; -NR .'.; -N+R R A.; -S.; -SO.; alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the RY radicals optionally may wherein the alkyl, polyalkyl, hatoalkyl, hydroxyalkyl, cycloalkyl,

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consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and wherein  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  are independently selected from the group wherein  $\mathbb{R}^7$  and  $\mathbb{R}^8$  are independently selected from the group

8 alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl;

wherein R13 and R14 together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

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wherein R<sup>14</sup> and R<sup>15</sup> together with the nitrogen atom to which they are attached form a cyclic ring; and

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wherein the R13, R14, and R15 alkyl; haloalkyl; cycloalkyl; polyalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether alkenyl; alkynyl; aryl; heterocyclyl; quatemary heterocyclyl; arylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; heterocyclylalkyl; quatemary heterocyclylalkyl; alkylarylalkyl;

heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; radicals optionally may be substituted with one or more radicals selected from OR16, -NR9R10, -NTR9R10RWA; -SR16, -S(O)R9; -SO2R9; -SO3R16; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary CO2R16, -CONR9R10, -SO2NR9R10, -PO(OR16)OR17, -PR9R10 the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; 8 55

wherein the R 13, R 14, and R 15 alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; P+R9R10R11A; -S+R9R10A-; and carbohydrate residue; and

radicals optionally may have one or more carbons replaced by -O-; -NR'-; -N+R9R<sup>10</sup>A:; -S.; -SO-; -SO<sub>2</sub>:, -S<sup>+</sup>R<sup>9</sup>A:-; -PR<sup>9</sup>-; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A:-; -P(O)R<sup>9</sup>-; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether phenylene; carbohydrate residue; amino acid residue; peptide residue; or alkyiheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; heterocyclylalkyl; quatemary heterocyclylalkyl; alkylarylalkyl; જ 2

wherein R 16 and R 17 are independently selected from the group consisting of R9 and M; and polypeptide residue; and

wherein R, R10, R11, R12, R, and A are as defined in claim 2. wherein M is a pharmaceutically acceptable cation; and

A compound of claim 2 wherein at least one of  $\mathbb{R}^5$  and  $\mathbb{R}^6$  has ≓ the formula

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wherein R' and t are defined as in claim 10.

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12. A compound of claim 11 wherein R" is selected from the group consisting of hydrogen, alkyl and aralkyl. A compound of claim 11 wherein RN is selected from the group consisting of hydrogen, (C1-C10)alkyl and aryl(C1-C10)alkyl A compound of claim 11 wherein R<sup>N</sup> is selected from the group consisting of hydrogen, methyl, ethyl and benzyl.

A compound of claim 11 wherein R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of hydrogen, alkyl, and (C,-C,0)cycloalkyl A compound of claim 11 wherein  $\mathbb{R}^1$  and  $\mathbb{R}^2$  are independently selected from the group consisting of hydrogen and (C<sub>1</sub>-C<sub>10</sub>)alkyl. <u>.</u>

A compound of claim 11 wherein R and R are independently selected from the group consisting of (CI-Cio)alkyl. A compound of claim 11 wherein R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of (C<sub>1</sub>-C<sub>7</sub>)alkyl.

A compound of claim 11 wherein R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of (C<sub>2</sub>-C<sub>4</sub>)alkyl. . 61

- selected from the group consisting ethyl; n-propyl; n-butyl; and isobutyl. A compound of claim 11 wherein R1 and R2 are independently
- A compound of claim 11 wherein R1 and R2 are each n-butyl.
- the other of R' and R' is n-butyl A compound of claim 11 wherein one of  $\mathbb{R}^1$  and  $\mathbb{R}^2$  is ethyl and
- A compound of claim 11 wherein q is 1, 2, or 3
- 25. A compound of claim 11 wherein q is 1 or 2.
- 26. A compound of claim 11 wherein q is 1.
- selected from the group consisting of hydrogen and -OR? A compound of claim 11 wherein R3 and R4 are independently
- 28. A compound of claim 27 wherein R9 is hydrogen
- relationship to said structure of formula (II) 29. A compound of claim 28 wherein said hydroxy group is in a syn
- 7-, 8- and 9-positions of the benzo ring of the structure of formula (I) A compound of claim 11 wherein RX radicals are present at the
- or more of the 7-, 8-, or 9-positions of the benzo ring of the structure of A compound of claim 11 wherein an RX radical is present at one
- 7- and 9-positions of the benzo ring of the structure of formula (I) A compound of claim 11 wherein RX radicals are present at the

- 7-position of the benzo ring of the structure of formula (I). A compound of claim 11 wherein an RX radical is present at the
- NR14C(0)R13; heterocyclyl; polyalkyl; acyloxy; polyether; halogen; -OR <sup>13</sup>; -NR <sup>13</sup>R <sup>14</sup>; -NR <sup>13</sup>NR <sup>14</sup>R <sup>15</sup>; -N<sup>4</sup>R <sup>9</sup>R <sup>11</sup>R <sup>12</sup>A<sup>-</sup>; -SR <sup>13</sup>; -S<sup>+</sup>R <sup>13</sup>R <sup>14</sup>A; -CO<sub>2</sub>R <sup>13</sup>; and -14 independently selected from the group consisting of alkyl; aryl; cycloalkyl; A compound of claim 32 wherein said one or more RX are

-S<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A<sup>-</sup>; and  $-sr^{16}; -s(O)r^9; -sO_2r^9; -sO_3r^{16}; oxo; -CO_2r^{16}; -CN; halogen; -conr^9r^{10}; -so, nr^9r^{10}; -po(Or^{16})Or^{17}; -pr^9r^{10}; -p^+r^9r^{11}r^{12}A^-; or^{17}r^{19}r^{10}; -ro(Or^{16})Or^{17}; -ro(Or^{16$ wherein alkyl; aryl; cycloalkyl; heterocyclyl; polyalkyl; acyloxy; and polyether; can be further substituted with -OR  $^{16}$ , -NR  $^{9}$ R  $^{10}$ , -N  $^{4}$ R  $^{9}$ R  $^{10}$ R  $^{w}$ A  $^{-}$ ;

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wherein in RX, one or more carbons are optionally replaced by -O-; -NR  $^{13}$ , -N<sup>+</sup>R  $^{13}$ R  $^{14}$ A  $^{-}$ ; -S-; -SO-; -SO<sub>2</sub>: -S<sup>+</sup>R  $^{13}$ A  $^{-}$ ; -PR  $^{13}$ : -P(O)R  $^{13}$ : -P<sup>†</sup>R<sup>13</sup>R<sup>14</sup>A<sup>-</sup>.; phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; polyether; or polyalkyl; and

- 2 are optionally replaced by -O-; -NR<sup>9</sup>-; -N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-; -S-; -SO-; -SO<sub>2</sub>-; -S<sup>+</sup>R<sup>9</sup>A-; -PR<sup>9</sup>-; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-; or -P(O)R<sup>9</sup>-. residue; polypeptide residue; and carbohydrate residue; one or more carbons wherein in said polyalkyl; phenylene; amino acid residue; peptide
- heterocyclyl; polyalkyl; acyloxy; polyether; halogen; -OR  $^{13}$ ; -NR  $^{13}R^{14}$ ; -NR  $^{13}NR^{14}R^{15}$ ; -N $^{+}R^{9}R^{11}R^{12}A^{-}$ ; -SR  $^{13}$ ; -S $^{+}R^{13}R^{14}A^{-}$ ; -CO2R  $^{13}$ ; and -NR<sup>14</sup>C(0)R<sup>13</sup>; independently selected from the group consisting of alkyl; aryl; cycloalkyl; A compound of claim 33 wherein said one or more RX are
- 5 wherein alkyl; aryl; cycloalkyl; heterocyclyl; polyalkyl; acyloxy; and polyether; can be further substituted with -OR <sup>16</sup>, -NR <sup>9</sup>R <sup>10</sup>, -N <sup>+</sup>R <sup>9</sup>R <sup>10</sup>R <sup>w</sup>A <sup>-</sup>;  $-SR^{16}; -S(O)R^9; -SO_2R^9; -SO_3R^{16}; oxo; -CO_2R^{16}; -CN; halogen; -CONR^9R^{10}; -SO_1NR^9R^{10}; -PO(OR^{16})OR^{17}; -PR^9R^{10}; -P^+R^9R^{11}R^{12}A^-; orconR^9R^{10}; -PR^9R^{10}; -PR^{10}; -PR^9R^{10}; -PR^{10}; -PR^{10}; -PR^{10}; -PR^{10}; -PR^{1$ -S<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A<sup>-</sup>; and
- wherein in RX, one or more carbons are optionally replaced by -O-; -NR  $^{13}$ ; -N $^+$ R  $^{13}$ R  $^{14}$ A  $^-$ ; -S-; -SO-; -SO2-; -S $^+$ R  $^{13}$ A -; -PR  $^{13}$  : -P(O)R  $^{13}$  -; -P

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 ${
m P}^+{
m R}^{13}{
m R}^{14}{
m A}^-$ ; phenylene; amino acid residue; peptide residue; polypeptide residue, polyelher; or polyalkyl; and

wherein in said polyalkyl; phenylene; amino acid residue; peptide residue; polypeptide residue; and carbohydrate residue; one or more carbons are optionally replaced by -O.; -NR $^9$ .; -N^R $^9$ R $^1$ O<sub>4</sub>.; -S.; -SO.; -SO<sub>2</sub>.: S<sup>+</sup>R $^9$ A.:, -PR $^9$ .; -PR $^9$ R $^1$ OA.; or -P(O)R $^9$ .

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- 36. A compound of claim 34 wherein said one or more R¹ are independently selected from the group consisting of polyether, -OR  $^{13}$ , -NR  $^{13}$ R  $^{14}$ , and -N^R  $^{2}$ R  $^{11}$ R  $^{12}$ A.
- 37. A compound of the claim 35 wherein said  $R^x$  is selected from the group consisting of polyether, -OR  $^{13}$ ; -NR  $^{13}R_1^4$ ; and -N^R $^9R_1^1R_1^2A$ .
- 38. A compound of claim 36 wherein said one or more R' are independently selected from the group consisting of -OR  $^{13}$  and -NR  $^{13}$ R  $^{14}$ .
- 39. A compound of claim 37 wherein said  $\rm R^x$  is independently selected from the group consisting of -OR  $^{13}$  and -NR  $^{13}\rm R^{14}$  .
- 40. A compound of claim 38 wherein R 13 and R 14 are each methyl.
- 41. A compound of the claim 39 wherein  $\mathbb{R}^{13}$  and  $\mathbb{R}^{14}$  are each methyl.
- 42. A compound of claim 11 wherein an  $\mathbb{R}^{y}$  substituent is attached at the 3- or the 4-position of the phenyl ring of the structure of formula (II).
- 13. A compound of claim 11 wherein t is 1 or 2.
- 44. A compound of claim 42 wherein t is 1 or 2.
- A compound of claim 11 wherein said one or more R<sup>y</sup> are independently selected from the group consisting of hydrogen; halogen; hydroxy, -NO2; (C,-C<sub>10</sub>)alkyl; halo(C,-C<sub>10</sub>)alkyl; aryl(C,-C<sub>10</sub>)alkyl;

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heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; polyether, -OR  $^{13};$  -NR  $^{13}R^{14};$  and -NR  $^{13}C(O)R^{14};$  and

and wherein  $R^{13}$ ,  $R^{14}$ , and  $R^{15}$  are independently selected from the group

whetein R , R , and R are independently selected from the group consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylhilterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl;

10 (C<sub>1</sub>-C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether, or wherein the R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary

heterocyclyi; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyi; halo(C<sub>1</sub>-C<sub>10</sub>)alkyi; heterocyclyi(C<sub>1</sub>-C<sub>10</sub>)alkyi; quaternary heterocyclyi(C<sub>1</sub>-C<sub>10</sub>)alkyi; (C<sub>1</sub>-C<sub>10</sub>)alkyil; (C<sub>1</sub>-C<sub>10</sub>)alkyilantmonium(C<sub>1</sub>-C<sub>10</sub>)alkyi; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; (C<sub>1</sub>-C<sub>10</sub>)alkyi; heterocyclyi; quaternary heterocyclyi; quaternary heterocyclyi; quaternary heterocyclyi; carboxy; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyi; -OR <sup>16</sup>; -NR <sup>9</sup>R <sup>10</sup>; -Nr <sup>9</sup>R <sup>10</sup>; and -CONR <sup>9</sup>R <sup>10</sup>; and

wherein R<sup>9</sup>, R<sup>10</sup>, and R<sup>w</sup> are independently selected from the group consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; ammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; carbo(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxyleterocyclyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkylamino; and acyl; and

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wherein A is a pharmaceutically acceptable anion; and wherein R 11 and R 12 are independently selected from the group consisting of hydrogen; (C,-C<sub>10</sub>)alky); heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; and carbo(C<sub>1</sub>-C<sub>10</sub>)alkyl; or

 $R^{11}$  and  $R^{12}$  together with the carbon atom to which they are attached form a cyclic ring; and wherein  $R^{16}$  and  $R^{17}$  are independently selected from the group

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consisting of R<sup>9</sup> and M; and wherein M is a pharmaceutically acceptable cation.

46. A compound of claim 11 wherein said R<sup>V</sup> is independently selected from the group consisting of hydrogen, chloro, fluoro, bromo, iodo, hydroxy, methoxy, nitro, amino, methylamino, dimethylamino, ethylamino, diethylamino, trimethylaminon, trichylaminonium,

trimethylammoniummethylcarbonylamino,

- triethylammoniumpropylcarbonylamino, trimethylammoniumbutylcarbonylamino, triethylammoniumbutylcarbonylamino, methylcarbonylamino, chloromethylcarbonylamino, fluoromethylcarbonylamino, bromomethylcarbonylamino, iodomethylcarbonylamino, ethylcarbonylamino,
- 15 chloroethylcarbonylamino, fluoroethylcarbonylamino, bromoethylcarbonylamino, iodoethylcarbonylamino, propylcarbonylamino, chloropropylcarbonylamino, fluoropropylcarbonylamino, bromopropylcarbonylamino, iodopropylcarbonylamino, butylcarbonylamino, chlorobutylcarbonylamino, fluorobutylcarbonylamino,
- 20 bromobutylcarbonylamino, iodobutylcarbonylamino, methoxycarbonyl, ethoxycarbonyl, trimethylammoniumethoxyethoxyethoxy, triethylammoniumethoxyethoxy, chloroethoxyethoxyethoxy, fluoroethoxyethoxyethoxy, bromoethoxyethoxy, iodoethoxyethoxy, pyridiniumethoxyethoxyethoxy,
- piperazinyloxymethoxyethoxy, methylpiperazinyloxymethoxyethoxy, dimethylpiperazinyloxymethoxyethoxyethoxy, piperidinyloxymethoxyethoxy, methylpiperidinyloxymethoxyethoxy, and dimethylpiperidinyloxymethoxyethoxyethoxyphenyl.

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- 47. A compound of claim 11 wherein said one or more RY are independently selected from the group consisting of hydroxy, methoxy, ethoxy, nitro, amino, methylamino, dimethylamino, ethylamino, diethylamino, trimethylammonium, triethylammonium,
- trimethylammoniummethylcarbonylamino, triethylammoniummethylcarbonylamino, triethylammoniumethylcarbonylamino, trimethylammoniumethylcarbonylamino, triethylammoniumethylcarbonylamino, trimethylammoniumpropylcarbonylamino,

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- triethylammoniumpropylcarbonylamino,
  trimethylammoniumbutylcarbonylamino,
  triethylammoniumbutylcarbonylamino, methylcarbonylamino,
  chloromethylcarbonylamino, fluoromethylcarbonylamino,
  bromomethylcarbonylamino, iodomethylcarbonylamino, ethylcarbonylamino
  tchloroethylcarbonylamino, fluoroethylcarbonylamino,
- bromoethylcarbonylamino, iodoethylcarbonylamino, propylcarbonylamino, chloropropylcarbonylamino, fluoropropylcarbonylamino, butylcarbonylamino, bromopropylcarbonylamino, iodopropylcarbonylamino, butylcarbonylamino, chlorobutylcarbonylamino, fluorobutylcarbonylamino, butylcarbonylamino, bromobutylcarbonylamino, fluorobutylcarbonylamino, iodobutylcarbonylamino, trimethylammoniumethoxyethoxyethoxy, chloroethoxyethoxyethoxy, fluoroethoxyethoxyethoxyethoxyethoxy, bromoethoxyethoxyethoxy, fluoroethoxyethoxyethoxy, and pyridiniumethoxyethoxyethoxyethoxy.
- 48. A compound of claim 11 wherein said one or more R<sup>y</sup> are independently selected from the group consisting of trimethylammonium, triethylammoniummethylammoniummethylammoniummethylammoniummethylamino, triethylammoniumethylambonylamino, triethylammoniumethylambonylamino, triethylammoniumpropylabonylamino, triethylammoniumpropylabonylamino, triethylammoniumpropylabonylamino, triethylammoniumbutylabonylamino, triethylammoniumbutylabonylamino, triethylammoniumbutylabonylamino, triethylammoniumbutylabonylamino, triethylammoniumbutylabonylamino,

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triethylammoniumethoxyethoxyethoxy.

- A compound of claim 11 wherein:
   R<sup>N</sup> is selected from the group consisting of hydrogen, alkyl and aralkyl;
- R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of hydrogen, alkyl, and (C<sub>2</sub>-C<sub>10</sub>)cycloalkyl.

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A compound of claim 11 wherein:

R" is selected from the group consisting of hydrogen, alkyl and aralkyl;

and

R³ and R⁴ are independently selected from the group consisting of

hydrogen and hydroxy.

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A compound of claim 50 wherein said hydroxy group is in a syn relationship to said structure of formula (II).

52. A compound of claim 11 wherein:

RN is selected from the group consisting of hydrogen, alkyl and aralkyl;

 $\mathbb{R}^{\mathbf{X}}$  is selected from the group consisting of polyether;  $-\mathsf{OR}^{13}$ ; -

arg

NR13R14; and -N+R9R11R12A-;

S

wherein R9, R11, R12, R13 and R14 are as defined in claim 2.

A compound of claim 11 wherein:

and R4 are independently selected from the group consisting of hydrogen and R 1 and R 2 are independently selected from the group consisting of hydrogen, alkyl, and (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl; and hydroxy.

is selected from the group consisting of polyether, -OR13; -NR13R14; and -54. A compound of claim 11 wherein:  $R^1 \text{ and } R^2 \text{ are independently selected from the group consisting of }$ hydrogen, alkyl, and (C<sub>3</sub>-C<sub>10</sub>)cycloalkyl; and N+R9R11R12A:

wherein R, R11, R12, R13 and R14 are as defined in claim 2.

55. A compound of claim 11 wherein:

R3 and R4 are independently selected from the group consisting of hydrogen and hydroxy; and

RX is selected from the group consisting of polyether; -OR 13; -NR 13R 14; and -N+R9R 11R 12A;

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wherein R9, R11, R12, R13 and R14 are as defined in claim 2.

A compound of claim 11 wherein:

RN is selected from the group consisting of hydrogen, alkyl and aralkyl; R1 and R2 are independently selected from the group consisting of hydrogen, alkyl, and (C3-C10)cycloalkyl; and

and R4 are independently selected from the group consisting of hydrogen and

hydroxy.

R" is selected from the group consisting of hydrogen, alkyl and aralkyl; R and R are independently selected from the group consisting of 57. A compound of claim 11 wherein: hydrogen, alkyl, and (C3-C10)cycloalkyl; and

is selected from the group consisting of polyether, -OR13; -NR13R14; and -N+R9R11R12A:

wherein R, R", R12, R13 and R14 are as defined in claim 2.

58. A compound of claim 11 wherein:

R" is selected from the group consisting of hydrogen, alkyl and aralkyl; R3 and R4 are independently selected from the group consisting of hydrogen and hydroxy; and

RX is selected from the group consisting of polyether, -OR 13; wherein R, R1, R12, R13 and R14 are as defined in claim 2. NR13R14; and -N+R9R11R12A;

A compound of claim 11 wherein: 59.

R and R are independently selected from the group consisting of hydrogen, alkyl, and (C3-C10)cycloalkyl;

R3 and R4 are independently selected from the group consisting of

hydrogen and hydroxy; and

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 $R^{\mathbf{X}}$  is selected from the group consisting of polyether, -OR  $^{13}$ ; -NR 13R 14; and -N+R9R 11R 12A-;

wherein R9, R11, R12, R13 and R14 are as defined in claim 2.

A compound of claim 11 wherein:

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 $R^N$  is selected from the group consisting of hydrogen, alkyl and aralkyl;  $R^1$  and  $R^2$  are independently selected from the group consisting of hydrogen, alkyl, and  $(C_3 - C_{10})$ cycloalkyl;  $R^3$  and  $R^4$ 

are independently selected from the group consisting of hydrogen and hydroxy;

 $R^X$  is selected from the group consisting of polyether; -OR  $^{13}$  , -NR  $^{13}R^{14}$  ; and -N  $^{+}R^{9}R^{11}R^{12}A^{-}$  ;

wherein R, R1, R1, R13 and R14 are as defined in claim 2.

- 61. A compound of claim 60 wherein  $\mathbb{R}^N$  is selected from the group consisting of hydrogen,  $(C_1\text{-}C_{10})$ alkyl and aryl $(C_1\text{-}C_{10})$ alkyl.
- 62. A compound of claim 60 wherein R<sup>N</sup> is selected from the group consisting of hydrogen, methyl, ethyl and benzyl.
- 63. A compound of claim 60 wherein R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of hydrogen and (C<sub>1</sub>-C<sub>10</sub>)alkyl.
- 64. A compound of claim 60 wherein  $\mathbb{R}^1$  and  $\mathbb{R}^2$  are independently selected from the group consisting of  $(C_i-C_{10})$  alkyl.
- 65. A compound of claim 60 wherein  $\mathbb{R}^1$  and  $\mathbb{R}^2$  are independently selected from the group consisting of  $(C_2 C_4)$ alky!.
- 66. A compound of claim 60 wherein R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting ethyl; n-propyl; n-butyl; and isobutyl.
- A compound of claim 60 wherein R<sup>1</sup> and R<sup>2</sup> are each n-butyl
- 68. A compound of claim 60 wherein one of  $\mathbb{R}^1$  and  $\mathbb{R}^2$  is ethyl and the other of  $\mathbb{R}^1$  and  $\mathbb{R}^2$  is n-butyl.
- A compound of claim 60 wherein q is 1, 2, or 3.
- 70. A compound of claim 60 wherein q is 1 or 2.

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- 71. A compound of claim 60 wherein q is 1.
- 72. A compound of claim 60 wherein R<sup>X</sup> radicals are present at the 7-, 8- and 9-positions of the benzo ring of the structure of formula (I).
- 73. A compound of claim 60 wherein an R<sup>X</sup> radical is present at one or more of the 7-, 8-, or 9-positions of the benzo ring of the structure of formula (I).
- A compound of claim 60 wherein R<sup>X</sup> radicals are present at the
   and 9-positions of the benzo ring of the structure of formula (f).
- 75. A compound of claim 60 wherein an R<sup>X</sup> radical is present at the 7-position of the benzo ring of the structure of formula (I).
- 76. A compound of claim 60 wherein said one or more R\* are independently selected from the group consisting of -OR <sup>13</sup> and -NR <sup>13</sup>R <sup>14</sup> wherein R<sup>13</sup> and R<sup>14</sup> are as defined in claim 2..
- 77. A compound of claim 76 wherein  $\mathbb{R}^{13}$  and  $\mathbb{R}^{14}$  are each methyl.
- 78. A compound of claim 60 wherein an  $\mathbb{R}^{Y}$  substituent is independently attached at the 3- or the 4-position of the phenyl ring of formula (II).
- 79. A compound of claim 60 wherein t is 1 or 2.
- 80. A compound of claim 60 wherein t is 1.
- 81. A compound of claim 60 wherein said one or more R<sup>y</sup> are independently selected from the group consisting of hydrogen; halogen; hydroxy; -NO<sub>2</sub>; (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; polyether; -OR <sup>13</sup>; -NR <sup>13</sup>R <sup>14</sup>; and -NR <sup>13</sup>C(O)R <sup>14</sup>; and

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wherein R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> are independently selected from the group consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl;

(C<sub>1</sub>-C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether; or wherein the R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; -OR<sup>16</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N\*R<sup>9</sup>R<sup>10</sup>R\*\*, and -CONR<sup>9</sup>R<sup>10</sup>; and

wherein R<sup>9</sup>, R<sup>10</sup>, and R<sup>w</sup> are independently selected from the group

consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>alkyl; heterocyclyl; armonium(C<sub>1</sub>-C<sub>10</sub>)alkyl;

(C<sub>1</sub>-C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>
C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; carbo(C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>1</sub>-C<sub>10</sub>)alkyl;

carboxyheterocyclyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkylamino; and acyl; and

wherein A' is a pharmaceutically acceptable anion; and

wherein R<sup>11</sup> and R<sup>12</sup> are independently selected from the group

consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl;

carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; and carbo(C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; or

R<sup>11</sup> and R<sup>12</sup> together with the carbon atom to which they are attach

R<sup>11</sup> and R<sup>12</sup> together with the carbon atom to which they are attached form a cyclic ring; and wherein R<sup>16</sup> and R<sup>17</sup> are independently selected from the group

wherein M is a pharmaceutically acceptable cation.

consisting of R and M; and

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82. A compound of claim 60 wherein said R<sup>y</sup> is independently selected from the group consisting of hydrogen, chloro, fluoro, bromo, iodo, hydroxy, methoxy, ethoxy, nitro, amino, methylamino, dimethylamino, ethylamino, diethylamino, trimethylammonium, triethylammonium, trimethylammonium,

trimethylammoniummethylcarbonylamino, triethylammoniummethylcarbonylamino, trimethylammoniumethylcarbonylamino,

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triethylammoniumethylcarbonylamino, trimethylammoniumpropylcarbonylamino,

10 triethylammoniumpropylcarbonylamino, trimethylammoniumbutylcarbonylamino, triethylammoniumbutylcarbonylamino, methylcarbonylamino, chloromethylcarbonylamino, fluoromethylcarbonylamino, bromomethylcarbonylamino, iodomethylcarbonylamino, ethylcarbonylamino,

15 chloroethylcarbonylamino, fluoroethylcarbonylamino, bromoethylcarbonylamino, iodoethylcarbonylamino, propylcarbonylamino, chloropropylcarbonylamino, fluoropropylcarbonylamino, bromopropylcarbonylamino, iodopropylcarbonylamino, butylcarbonylamino, chlorobutylcarbonylamino, fluorobutylcarbonylamino,

bromobutylcarbonylamino, iodobutylcarbonylamino, methoxycarbonyl, ethoxycarbonyl, trimethylammoniumethoxyethoxyethoxy, triethylammoniumethoxyethoxy, chloroethoxyethoxy, fluoroethoxyethoxyethoxy, bromoethoxyethoxy, iodoethoxyethoxyethoxy, pyridiniumethoxyethoxyethoxy, pyridiniumethoxyeth

piperazinyloxymethoxyethoxy, methylpiperazinyloxymethoxyethoxyethoxy, dimethylpiperazinyloxymethoxyethoxyethoxy, piperidinyloxymethoxyethoxy, methylpiperidinyloxymethoxyethoxy, and

dimethylpiperidinyloxymethoxyethoxyethoxyphenyl.

83. A compound of claim 60 wherein said one or more R<sup>y</sup> are independently selected from the group consisting of hydroxy, methoxy, nitro, amino, methylamino, dimethylamino, ethylamino, diethylamino, trimethylammonium, triethylammoniummethylcarbonylamino, triethylammoniummethylcarbonylamino, triethylammoniummethylcarbonylamino, triethylammoniumethylcarbonylamino, triethylammoniumethylcarbonylamino, triethylammoniumethylcarbonylamino, triethylammoniumpopylcarbonylamino, triethylammoniumpopylcarbonylamino,

 triethylammoniumpropylcarbonylamino, trimethylammoniumbutylcarbonylamino,

bromopropylcarbonylamino, iodopropylcarbonylamino, butylcarbonylamino chloropropylcarbonylamino, fluoropropylcarbonylamino, bromoethylcarbonylamino, iodoethylcarbonylamino, propylcarbonylamino, chloroethylcarbonylamino, fluoroethylcarbonylamino,

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triethylammoniumethoxyethoxyethoxy, chloroethoxyethoxyethoxy, bromobutylcarbonylamino, iodobutylcarbonylamino, trimethylammoniumethoxyethoxyethoxy, iodoethoxyethoxyethoxy, and pyridiniumethoxyethoxyethoxy. fluoroethoxyethoxyethoxy, bromoethoxyethoxyethoxy,

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chlorobutylcarbonylamino, fluorobutylcarbonylamino,

- trimethylammoniumethylcarbonylamino, triethylammoniummethylcarbonylamino, triethylammonium, trimethylammoniummethylcarbonylamino, independently selected from the group consisting of trimethylammonium, A compound of claim 60 wherein said one or more RY are
- trimethylammoniumethoxyethoxyethoxy, and triethylammoniumbutylcarbonylamino, trimethylammoniumbutylcarbonylamino, triethylammoniumethoxyethoxyethoxy. triethylammoniumpropylcarbonylamino, trimethylammoniumpropylcarbonylamino, triethylammoniumethylcarbonylamino,

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- relationship to said structure of formula (II) A compound of claim 60 wherein said hydroxy group is in a syn
- 86. A compound of formula (I):

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R<sup>3</sup> is hydroxy; R and R are each independently alkyl; q is 1 or 2; R4 and R6 are hydrogen;

R<sup>2</sup> has the formula (II):

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wherein t is an integer from 0 to 5;

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hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; -OR <sup>13</sup>; -NR <sup>13</sup>R <sup>14</sup>, SR <sup>13</sup>; -S(O)R <sup>13</sup>; -SO<sub>2</sub>R <sup>13</sup>; -SO<sub>3</sub>R <sup>13</sup>; -NR <sup>13</sup>OR <sup>14</sup>; -NR <sup>13</sup>NR <sup>14</sup>R <sup>15</sup>; NR<sup>13</sup>SO,NR<sup>14</sup>R<sup>15</sup>,-P(O)R<sup>13</sup>R<sup>14</sup>;-PR<sup>13</sup>R<sup>14</sup>,-PR<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>-</sup>;-P(OR<sup>13</sup>)OR<sup>14</sup>;-S<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A<sup>-</sup>; and -N<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>-</sup>; and OC(O)NR13R14; -NR13SOR14; -NR13SO,R14; -NR13SONR14R15; - $CO_2R^{13}$ ; -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>; -C(O)NR<sup>13</sup>R<sup>14</sup>; -C(O)OM; COR<sup>13</sup>; -NR<sup>13</sup>C(O)R<sup>14</sup>; -NR<sup>13</sup>C(O)NR<sup>14</sup>R<sup>15</sup>; -NR<sup>13</sup>CO,R<sup>14</sup>; -OC(O)R<sup>13</sup>; hydrogen; halogen; -CN; -NO2; oxo; alkyl; polyalkyl; haloalkyl; one or more RY are independently selected from the group consisting of

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wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R<sup>y</sup> radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclylalkyl; quaternary heterocyclyl; -OR <sup>7</sup>; -NR <sup>7</sup>R, -SR), -S(O)R <sup>7</sup>; -SO2R <sup>7</sup>; -SONR <sup>7</sup>; -SONR <sup>7</sup>; -SONR <sup>7</sup>; -SONR <sup>7</sup>; -R <sup>8</sup>, -PR <sup>7</sup>R <sup>8</sup>R <sup>9</sup>A <sup>7</sup>; and -P(O)(OR <sup>7</sup>)OR <sup>8</sup>; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, blankyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R<sup>Y</sup> radicals optionally may have one or more carbons replaced by -O.; -NR<sup>7</sup>; -N<sup>+</sup>R<sup>3</sup>R<sup>4</sup>·· -S.; -SO·; -SO<sub>2</sub>·· -S<sup>+</sup>R<sup>7</sup>A··; -PR<sup>7</sup>·· -P(O)R<sup>7</sup>·· -P<sup>+</sup>R<sup>7</sup>R<sup>8</sup>A··; or phenylene; and

wherein R<sup>7</sup> and R<sup>8</sup> are independently selected from the group consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and wherein R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl;

consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl;
alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl;
heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl;
60 alkylheterocyclylalkyl; alkylarnmoniumalkyl; aminocarbonylalkyl;
alkylarninocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R<sup>13</sup> and R<sup>14</sup> together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein  $R^{14}$  and  $R^{15}$  together with the nitrogen atom to which they are attached form a cyclic ring; and

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wherein the R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylarylalkyl; alkylarmoniumalkyl; aminocarbonylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylammocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl;

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hydroxyalkyi; sulfoalkyi, alkenyi; alkynyi, aryi; heterocyclyi; quaternary heterocyclyi, quaternary heterocyclyii; carboxy; carboxyalkyi; guaniqinyi; -OR<sup>16</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>w</sup>A; -SR<sup>16</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>2</sub>R<sup>16</sup>; -CO<sub>2</sub>R<sup>16</sup>; -CO<sub>2</sub>R<sup>16</sup>; -CO<sub>2</sub>R<sup>16</sup>; -CO<sub>2</sub>R<sup>16</sup>; -PO(OR<sup>16</sup>)OR<sup>17</sup>; -PR<sup>9</sup>R<sup>10</sup>; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>; -P<sup>+</sup>R<sup>10</sup>; -P<sup>+</sup>R<sup>1</sup>

wherein the R <sup>13</sup>, R <sup>14</sup>, and R <sup>15</sup> alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylheterocyclylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; -NR\*-. N<sup>+</sup>R<sup>9</sup>R <sup>10</sup>A-; -S-; -SO-; -SO<sub>2</sub>: -S<sup>+</sup>R<sup>9</sup>A-: -PR<sup>9</sup>; -P<sup>+</sup>R<sup>9</sup>R <sup>10</sup>A-; -P(O)R\*, phenylene; carbohydrate residue; amino acid residue; peptide residue; or

wherein R<sup>16</sup> and R<sup>17</sup> are independently selected from the group consisting of R<sup>9</sup> and M; and

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polypeptide residue; and

wherein M is a pharmaceutically acceptable cation; and wherein R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>2</sup>, and A<sup>2</sup> are as defined in claim 2; and R<sup>N</sup> is selected from the group consisting of hydrogen; alkyl; and aralkyl; and

one or more  $\mathbb{R}^{\mathbf{X}}$  radicals are independently selected from the group consisting of alkoxy, alkylamino and dialkylamino; or

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a pharmaceutically acceptable salt, solvate, or prodrug thereof.

87. A compound of claim 86 wherein R<sup>1</sup> and R<sup>2</sup> are each the same (C<sub>1</sub>-C<sub>10</sub>)alkyl.

88. A compound of claim 86 wherein R1 and R2 are each n-butyl.

89. A compound of claim 86 wherein one or more R¹ are independently selected from the group consisting of methoxy and dimethylamino.

90. A compound of claim 86 wherein q is 1.

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91. A compound of claim 86 wherein q is 1, and R\* is selected from the group consisting of methoxy and dimethylamino.

- 92. A compound of claim 86 wherein R<sup>N</sup> is selected from thegroup consisting of hydrogen; methyl, ethyl and benzyl.
- A compound of claim 86 wherein said hydroxy group is in a sym relationship to said structure of formula (II).
- 94. A compound of claim 86 wherein t is 1.
- 95. A compound of claim 86 wherein t is 1 and  $R^{\gamma}$  is in the para position.
- A compound of claim 86 wherein t is 1 and R' is in the meta position.
- 97. A compound of claim 86 wherein one or more R' are independently selected from selected from the group consisting of halogen; hydroxy; -NO2: (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; polyether; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; and -NR<sup>13</sup>C(O)R<sup>14</sup>; and wherein R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> are independently selected from the group
- wherein  $\mathbb{R}^{1.3}$ ,  $\mathbb{R}^{1.4}$ , and  $\mathbb{R}^{1.3}$  are independently selected from the group consisting of hydrogen;  $(C_1\text{-}C_{10})$ alkyl; halo $(C_1\text{-}C_{10})$ alkyl; heterocyclyl; quaternary heterocyclyl; aryl $(C_1\text{-}C_{10})$ alkyl; heterocyclyl $(C_1\text{-}C_{10})$ alkyl; quaternary heterocyclyl $(C_1\text{-}C_{10})$ alkyl;  $(C_1\text{-}C_{10})$ alkylheterocyclyl $(C_1\text{-}C_{10})$ alkyl; and polyether; or
- (C<sub>1</sub>-C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether, or wherein the R <sup>13</sup>, R <sup>14</sup>, and R <sup>15</sup> (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy; carbox

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wherein R<sup>9</sup>, R<sup>10</sup>, and R<sup>w</sup> are independently selected from the group consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; ammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkyl; armonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; carbo(C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxyleterocyclyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkylamino; and acyl; and wherein A<sup>-1</sup> is a pharmaceutically acceptable anion; and wherein R<sup>11</sup> and R<sup>12</sup> are independently selected from the group

- consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; and carbo(C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; or R<sup>11</sup> and R<sup>12</sup> together with the carbon atom to which they are attached form a cyclic ring; and wherein R<sup>16</sup> and R<sup>17</sup> are independently selected from the group
- 30 consisting of R<sup>9</sup> and M; and wherein M is a pharmaceutically acceptable cation.

98. A compound of claim 97 wherein:

R! and R<sup>2</sup> are each the same (C<sub>1</sub>-C<sub>10</sub>)alkyl;
one or more R\* are independently selected from the group consisting of methoxy and dimethylamino;
said hydroxy group is in a syn relationship to said structure of formula (II);
t is 1; and

99. A compound of claim 97 wherein R1 and R2 are each n-butyl.

Ry is in the meta or para position

- 100. A compound of claim 97 wherein q is 1
- 101. A compound of claim 97 wherein  $\mathbf{R}^{\mathbf{N}}$  is selected from the group consisting of hydrogen; methyl, ethyl and benzyl.
- A compound of claim 97 wherein R<sup>y</sup> is in the para position.
- 103. A compound of claim 97 wherein R' is in the meta position.

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104. A compound of the formula (III):

wherein:

q and r are independently integers from 0 to 4; t and u are independently integers from 0 to 4;

R<sup>1</sup>, R<sup>2</sup>, R<sup>1A</sup>, and R<sup>2A</sup> are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclyl; alkoxyalkyl; alkoxyalkyl; aryloxyalkyl; heterocyclyloxyalkyl; alkylaryl; and (polyalkyl)aryl; or

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 $R^1$  and  $R^2$  taken together with the carbon to which they are attached 15 form C<sub>3</sub>-C<sub>10</sub> cycloalkenyl; or

 $R^{1A}$  and  $R^{2A}$  taken together with the carbon to which they are attached form  $C_1$ - $C_{10}$  cycloalkyl or  $C_3$ - $C_{10}$  cycloalkenyl; wherein the  $R^1$ ,  $R^2$ ,  $R^{1A}$ , and  $R^{2A}$  alkyl; cycloalkyl; alkenyl;

cycloalkenyl; alkynyl; aryl; heterocyclyl; arylatkyl; heterocyclylalkyl;

alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl;

aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl;

heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may
be substituted with one or more radicals selected from the group consisting of
CN; halogen; oxo; -OR9; -NR9R10; -N<sup>+</sup>R9R10R<sup>M</sup>A; -SR9; -S'RPR10A; -

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25 PR<sup>9</sup>R<sup>10</sup>; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>w</sup>A<sup>-</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; and -CONR<sup>9</sup>R<sup>10</sup>; and

wherein the R<sup>1</sup>, R<sup>2</sup>, R<sup>1</sup>A, and R<sup>2</sup>A alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkyl; alkoxyalkyl; alkoxyalkyl; aryloxyalkyl; aryloxyalkyl; aryloxyalkyl; aryloxyalkyl; heterocycloxyalkyl; heterocycloxyalkyl;

30 aryloxyalkynyl; heterocyicyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may have one or more carbons replaced by -O.; -NR<sup>9</sup>; -N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-; -S.; -SO.; -SO2-; -S<sup>+</sup>R<sup>9</sup>A-: -PR<sup>9</sup>; -P(O)R<sup>9</sup>; -P<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A-; or phenylene; and wherein R<sup>9</sup>, R<sup>10</sup>, and R<sup>W</sup> are independently selected from the group

onsisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; arkoxyalkyl; carboxyalkyl; carboxyalkyl; arylalkyl; carboxyheterocyclyl; amino; alkylamino; carboxyalkylamino; alkoxyalkylamino; and acyl; and

wherein A is a pharmaceutically acceptable anion; and R<sup>3</sup>, R<sup>4</sup>, R<sup>3A</sup>, and R<sup>4A</sup> are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; -OR<sup>9</sup>, -NR<sup>9</sup>R<sup>10</sup>; -SR<sup>9</sup>, -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; and -SO<sub>3</sub>R<sup>9</sup>; or R<sup>3</sup> and R<sup>4</sup> together form =O, =NOR<sup>9</sup>; =S; =NNR<sup>9</sup>R<sup>10</sup>; =NR<sup>9</sup>; or

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=CR  $^{11}R^{12}$  , or  $^{R^{3A}}$  and  $^{R^{4A}}$  together form =O; =NOR  $^9$  ; =S; =NNR  $^9R^{10}$  ; =NR  $^9$  , or =CR  $^{11}R^{12}$  ,

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wherein R<sup>11</sup> and R<sup>12</sup> are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkoryl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; arkoxyalkyl; carboxlylkyl; cycloalkyl; cycloalkenyl; haloalkyl; hydroxyalkyl; cycloalkyl; cycloalkyl; cycloalkyl; -SN<sup>9</sup>; -SO<sub>3</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>9</sup>; and

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-CONR  $^9R^{10}$ ; or R  $^{12}$  together with the carbon atom to which they are attached form a cyclic ring; and

wherein  $\mathbb{R}^2$  and  $\mathbb{R}^{10}$  are as defined above; and

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one or more R<sup>y</sup> and R<sup>yA</sup> are independently selected from the group consisting of halogen; -CN; -NO2; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclyl; alkynyl; heterocyclyl; arylalkyl; heterocyclyl; alkynyl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; -OR <sup>13</sup>; -NR <sup>13</sup>R <sup>14</sup>; -

S 8  $CO_2R^{13}$ ; -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>NR  $^{13}R^{14}$ ; -C(O)NR  $^{13}R^{14}$ ; -C(O)OM; -OC(O)NR''R'', -NR''SOR'', -NR''SO,R'', -NR''SONR''R'', -NR''SO,NR''R'', -P(O)R<sup>13</sup>R<sup>14</sup>, -PR<sup>13</sup>R<sup>14</sup>, -P<sup>†</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A; -COR<sup>13</sup>; -NR<sup>13</sup>C(0)R<sup>14</sup>; -NR<sup>13</sup>C(0)NR<sup>14</sup>R<sup>15</sup>; -NR<sup>13</sup>CO<sub>2</sub>R<sup>14</sup>; -OC(0)R<sup>13</sup>; -SR<sup>13</sup>; -S(0)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -

8 heterocyclyl; -OR7; -NR7R8; -SR7; -S(O)R7; -SO2R7; -SO3R7; -CO2R7; -CONR7R8; -N†R7R8R9A; -P(O)R7R8; -PR7R8; -P†R7R8R9A; and -P(OR 13) OR 14; -S+R 13R 14A; and -N+R 13R 14R 15A; and P(O)(OR')OR'; and the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary optionally may be further substituted with one or more radicals selected from heterocyclylalkyl, and polyether substituents of the RY and RYA radicals alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl,

-; -S-; -SO-; -SO2-; -S<sup>T</sup>R'A-; -PR'-; -P(O)R'-; -P<sup>T</sup>R'R<sup>o</sup>A-; or phenylene optionally may have one or more carbons replaced by -O-; -NR -; -N +R 7R 8A. heterocyclylalkyl, and polyether substituents of the RY and RYA radicals alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl

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consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and wherein  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; wherein  $\mathbb{R}^7$  and  $\mathbb{R}^8$  are independently selected from the group

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attached form a mono- or polycyclic heterocyclyl that is optionally substituted alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; with one or more radicals selected from the group consisting of oxo, carboxy, heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; wherein R13 and R14 together with the nitrogen atom to which they are

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attached form a cyclic ring; and wherein R<sup>14</sup> and R<sup>15</sup> together with the nitrogen atom to which they are and quaternary salts; or

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8 9 -OR16,-NR9R10; NTR9R10RWA; SR16, S(O)R9; SO2R9; SO3R16, heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; hydroxyalkyi; sulfoalkyi; alkenyl; alkynyl; aryl; heterocyclyl; quaternary the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; radicals optionally may be substituted with one or more radicals selected from alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; wherein the  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  alkyl; haloalkyl; cycloalkyl; polyalkyl;

10 ខ្ល CO2R  $^{16}$ , -CONR  $^{9}$ R  $^{10}$ , -SO2NR  $^{9}$ R  $^{10}$ ; -PO(OR  $^{16}$ )OR  $^{17}$ ; -PR  $^{9}$ R  $^{10}$ , -P<sup>+</sup>R  $^{9}$ R  $^{10}$ R  $^{11}$ A-; -S<sup>+</sup>R  $^{9}$ R  $^{10}$ A-; and carbohydrate residue; and radicals optionally may have one or more carbons replaced by -O-; -NR2-; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; wherein the  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  alkyl; haloalkyl; cycloalkyl; polyalkyl;

15 polypeptide residue; and phenylene; carbohydrate residue; amino acid residue; peptide residue; or  $N^{\dagger}R^{9}R^{10}A^{-}; -S^{-}; -SO^{-}; -SO^{-}; -S^{\dagger}R^{9}A^{-}; -PR^{9}^{-}; -P^{\dagger}R^{9}R^{10}A^{-}; -P(O)R^{0};$ 

consisting of R and M; and wherein R 16 and R 17 are independently selected from the group

wherein n is 0, 1 or 2; and

 $\mathbb{R}^{N}$  and  $\mathbb{R}^{\mathsf{N}_{A}}$  are independently selected from the group consisting of wherein R9, R10, R11, R12, Rw, and A are as defined above; and wherein M is a pharmaceutically acceptable cation; and

hydrogen; alkyi; alkenyl; alkynyl; aralkyi; and heterocyclylalkyl; and

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125 uaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy; OR <sup>13</sup>, -NR <sup>13</sup>R <sup>14</sup>, -SR <sup>13</sup>, -S(O)R <sup>13</sup>, -S(O)R <sup>13</sup>, -SO<sub>3</sub>R <sup>13</sup>, -S<sup>+</sup>R <sup>13</sup>R <sup>14</sup>A.; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; NR<sup>13</sup>OR<sup>14</sup>, -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>, -CO<sub>2</sub>R<sup>13</sup>, -OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>, -NR''C(O)R'<sup>13</sup>; -C(O)NR<sup>13</sup>R<sup>14</sup>, -C(O)OM; -COR<sup>13</sup>; -OR<sup>18</sup>, -SO<sub>2</sub>NR<sup>13</sup>R<sup>18</sup> group consisting of hydrogen; halogen; -CN; -NO2; alkyl; cycloalkyl; one or more RX and RXA radicals are independently selected from the

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130 NR  $^{18}$ OR  $^{14}$ ; -N $^+$ R  $^{13}$ R  $^{14}$ R  $^{15}$ A $^-$ ; -PR  $^{13}$ R  $^{14}$ , -P(O)R  $^{13}$ R  $^{14}$ R  $^{15}$ A $^-$ ; amino acid residue; peptide residue; polypeptide residue; and carbohydrate residue;

wherein the R<sup>x</sup> and R<sup>xA</sup> alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; beterocyclylalkyl; polyether; acyloxy radicals optionally may be further substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; -OR<sup>16</sup>, -NR<sup>9</sup>R<sup>10</sup>; -N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>R<sup>4</sup>M<sup>-7</sup>; -SR<sup>16</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>2</sub>R<sup>16</sup>; -CO<sub>2</sub>R<sup>16</sup>; -CONR<sup>9</sup>R<sup>10</sup>; -PO(OR<sup>19</sup>)OR<sup>17</sup>; -PR<sup>9</sup>R<sup>10</sup>; -P<sup>+</sup>R<sup>9</sup>R<sup>11</sup>R<sup>12</sup>A<sup>-7</sup>; -S<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A<sup>-7</sup>; and carbohydrate residue; and

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wherein the R<sup>x</sup> and R<sup>xA</sup> quaternary heterocyclyl radical optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; -NO2; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; -OR 1<sup>3</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR 1<sup>3</sup>; -S(O)R 1<sup>3</sup>; -SO2R 1<sup>3</sup>; -SO3R 1<sup>3</sup>; -NR<sup>13</sup>OR 1<sup>4</sup>; -NR 1<sup>3</sup>NR 1<sup>4</sup>K 1<sup>5</sup>; -CO2R 1<sup>3</sup>; OODR 1<sup>3</sup>R 1<sup>4</sup>; -R 1<sup>3</sup>R 1<sup>4</sup>; -R 1<sup>3</sup>R 1<sup>4</sup>K 1<sup>5</sup>A; -P(O)R 1<sup>3</sup>; -P(O)R 1<sup>3</sup>R 1<sup>4</sup>; -P(O)R 1<sup>3</sup>R 1<sup>4</sup>; -R 1<sup>3</sup>R 1<sup>4</sup>R 1<sup>5</sup>A; and carbohydrate residue; and

wherein the R<sup>x</sup> and R<sup>xx</sup> radicals comprising carbon optionally may lave one or more carbons replaced by -O.: \( \text{N}\)^{1.2}. \( \text{N}\)^R \( \text{R}\)^1 \( \text{A}\) \( \text{C}\). \( \text{S}\) \( \text{S}\) \( \text{S}\) \( \text{S}\) \( \text{S}\) \( \text{S}\) \( \text{R}\) \( \t

wherein R<sup>18</sup> is selected from the group consisting of alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and

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wherein the R<sup>11</sup> alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl radicals optionally may be substituted with one or more radicals selected from the group consisting of

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165 halogen; -CN; NO;; oxo; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N<sup>4</sup>R<sup>9</sup>R<sup>11</sup>R<sup>12</sup>A; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -CO<sub>2</sub>R<sup>9</sup>; -CO<sub>3</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>9</sup>; -PR<sup>9</sup>R<sup>10</sup>; -P(OR<sup>16</sup>)OR<sup>17</sup>; and -C(O)OM; and

 alkyne diyl; polyalkane diyl; alkoxy diyl; polyether diyl; polyalkoxy diyl; carbohydrate; amino acid; and peptide; polypeptide; wherein alkane diyl; alkene diyl; alkene diyl; polyalkane diyl; polyalkane diyl; alkene diyl; polyalkane diyl; alkene diyl; polyalkoxy diyl; polyalkane diyl; alkoxy diyl; polyalkoxy diyl; carbohydrate residue; amino acid residue; peptide residue; and polyalkoxy diyl; carbohydrate residue; amino acid residue; peptide residue; and polypeptide residue; can optionally have one or more carbons replaced by -O-; -NR 7; -N<sup>+</sup>R 7<sup>R</sup>8<sup>A</sup>-; -S·; -SO-; -SO<sub>2</sub>; -S<sup>+</sup>R 7<sup>A</sup>-; -P<sup>R</sup> 7<sup>R</sup>8<sup>A</sup>-; phenyleme; heterocyclyl; quaternary heterocyclyl; or aryl;

wherein alkane diyl; alkene diyl; alkyne diyl; polyalkane diyl; alkoxy diyl; polyelher diyl; polyalkoxy diyl; carbobydrate residue; amino acid residue; peptide residue; and polypeptide residue can be substituted with one or more substituent groups independently selected from the group consisting of alkyl; alkenyl; alkynyl; polyalkyl; polyether; aryl; haloalkyl; cycloalkyl; heterocyclyl; arylalkyl; halogen; oxo; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>, -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>, -NR<sup>13</sup>R<sup>14</sup>, -NR<sup>13</sup>CO<sub>3</sub>R<sup>13</sup>; -CO<sub>3</sub>R<sup>13</sup>; -CN; -OM; -

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wherein R', R', R', R', R', R', R', and A' are as defined above; or a pharmaceutically acceptable salt, solvate, or prodrug thereof.

105. A compound of claim 104 wherein R¹, R¹A, R², and R²A are independently selected from the group consisting of hydrogen and alkyl.

106. A compound of claim 104 wherein R¹, R¹, R², and R²A are independently selected from the group consisting of hydrogen and C₁-C₁₀ alkyl.

107. A compound of claim 104 wherein R¹, R¹, R², and R²A are independently selected from the group consisting of C<sub>2</sub>-C<sub>7</sub> alkyl.

- independently selected from the group consisting of C1-C, alkyl. 108. A compound of claim 104 wherein R<sup>1</sup>, R<sup>1</sup>, R<sup>2</sup>, and R<sup>2</sup> are
- and isobutyl. independently selected from the group consisting of ethyl; n-propyl; n-butyl; 109. A compound of claim 104 wherein R', R', R2, and R2 are
- independently selected from the group consisting of hydrogen and -OR?, wherein R9 is as defined in claim 104. 110. A compound of claim 104 wherein R3, R34, R4, and R44 are
- 111. A compound of claim 110 wherein R9 is hydrogen.
- independently selected from the group consisting of hydrogen, alkyl and 112. A compound of claim 104 wherein R<sup>N</sup> and R<sup>NA</sup> are
- and  $aryl(C_1-C_{10})alkyl$ . independently selected from the group consisting of hydrogen, (C<sub>1</sub>-C<sub>10</sub>)alkyl 113. A compound of claim 104 wherein R<sup>N</sup> and R<sup>NA</sup> are
- and benzyl. independently selected from the group consisting of hydrogen, methyl, ethyl 114. A compound of claim 104 wherein R<sup>N</sup> and R<sup>NA</sup> are
- independently selected from the group consisting of methoxy and dimethylamino 115. A compound of claim 104 wherein one or more R\* and R\*\* are
- 116. A compound of claim 104 wherein q and r are each 1.
- hydroxy; -NO2; (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; independently selected from selected from the group consisting of halogen; 117. A compound of claim 104 wherein one or more R' are

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heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; polyether; -OR <sup>13</sup>; -NR <sup>13</sup>R <sup>14</sup>; and -NR <sup>13</sup>C(O)R <sup>14</sup>;

consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; (C<sub>1</sub>-C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether; or quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylheterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; wherein  $R^{13}$ ,  $R^{14}$ , and  $R^{15}$  are independently selected from the group

5 C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether radicals C<sub>10</sub>)alkyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylheterocyclyl(C<sub>1</sub>heterocyclyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>wherein the  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  ( $C_i$ - $C_{io}$ )alkyl; halo( $C_i$ - $C_{io}$ )alkyl;

20 ᅜ heterocyclyl; quaternary heterocyclyl( $C_1$ - $C_{10}$ )alkyl; carboxy; carboxy( $C_1$ - $C_{10}$ )alkyl; -OR  $^{16}$ , -NR  $^{9}$ R  $^{10}$ , -N $^{+}$ R  $^{9}$ R  $^{10}$ R  $^{w}$ A ; and -CONR  $^{9}$ R  $^{10}$ ; and optionally may be substituted with one or more radicals selected from the carboxyheterocyclyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkylamino; and acyl; and C10)alkyl; carboxy(C1-C10)alkyl; carbo(C1-C10)alkoxy(C1-C10)alkyl; consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; ammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; group consisting of halogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary (C<sub>1</sub>-C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>wherein  $\mathbb{R}^9$ ,  $\mathbb{R}^{10}$ , and  $\mathbb{R}^W$  are independently selected from the group

ટ્ટ carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; and carbo(C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; or consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; form a cyclic ring  $\mathbb{R}^{11}$  and  $\mathbb{R}^{12}$  together with the carbon atom to which they are attached wherein  $\mathbb{R}^{11}$  and  $\mathbb{R}^{12}$  are independently selected from the group

wherein A is a pharmaceutically acceptable anion; and

30 consisting of R9 and M; and wherein  $\mathbb{R}^{16}$  and  $\mathbb{R}^{17}$  are independently selected from the group wherein M is a pharmaceutically acceptable cation

group consisting of alkane diyl; polyalkane diyl; alkoxy diyl; and polyalkoxy 118. A compound of claim 104 wherein R19 is selected from the

carbons replaced by -O-; -NR  $^7$ -; -N<sup>+</sup>R  $^7$ R  $^8$ A-; -S-; -SO-; -SO2-; -S<sup>+</sup>R  $^7$ A-; diyl; wherein alkane diyl and polyalkane diyl can optionally have one or more

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PR7.; -P(O)R7.; -P\*R7R8A.; or phenylene, wherein R7 and R8 are defined as in claim 104. Š

carbons are optionally replaced by -O-; -NR 7-; -N R A-; -S-; -SO-; -SO2-; 119. A compound of claim 104 wherein R<sup>19</sup> is selected from the -S<sup>+</sup>R<sup>7</sup>A<sup>--</sup>; -P(O)R<sup>7</sup>-; -P(O)R<sup>7</sup>-; phenylene; amino acid residue; group consisting of alkoxy diyl and polyalkoxydiyl wherein one or more peptide residue; polypeptide residue; carbohydrate residue; or polyalkyl,

A compound of claim 104 having the formula:

wherein R9 and R10 are defined as in claim 104.

121. A compound of the formula (IV):

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consisting of hydrogen; alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl;  $R^1,\,R^2,\,R^{1A},$  and  $R^{2A}$  are independently selected from the group heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; q and r are independently integers from 0 to 3; t and u are independently integers from 0 to 5; 13

heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; and (polyalkyl)aryl; or ន

form C<sub>3</sub>-C<sub>10</sub> cycloalkyl or C<sub>3</sub>-C<sub>10</sub> cycloalkenyl; or  $R^{1A}$  and  $R^{2A}$  taken together with the carbon to which they are attached R and R taken together with the carbon to which they are attached

alkoxyalkyi; alkoxyalkcnyl; alkoxyalkynyi; aryloxyalkyl; aryloxyalkcnyl; wherein the  $\rm R^1, \rm R^2, \rm R^{1A}$ , and  $\rm R^{2A}$  aikyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; form C<sub>3</sub>-C<sub>10</sub> cycloalkyl or C<sub>3</sub>-C<sub>10</sub> cycloalkenyl; 23

be substituted with one or more radicals selected from the group consisting of heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may CN; halogen; oxo; -OR?; -NR<sup>2</sup>R<sup>10</sup>; -N<sup>+</sup>R<sup>3</sup>R<sup>10</sup>R<sup>w</sup>A<sup>-</sup>; -SR<sup>9</sup>; -S<sup>\*</sup>R<sup>3</sup>R<sup>10</sup>A<sup>-</sup>; -PR<sup>3</sup>R<sup>10</sup>; -P<sup>+</sup>R<sup>3</sup>R<sup>10</sup>R<sup>w</sup>A<sup>-</sup>; -S(O)R<sup>3</sup>; -SO<sub>2</sub>R<sup>3</sup>; -SO<sub>3</sub>R<sup>3</sup>; -CO<sub>2</sub>R<sup>3</sup>; and aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; 2 33

CONR9R10; and

aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; wherein the  $R^1$ ,  $R^2$ ,  $R^{1A}$ , and  $R^{2A}$  alkyl; cycloalkyl; alkenyl;

 $SO_2$ :  $-S^{\dagger}R^9A^-$ ;  $-PR^9$ ;  $-P(O)R^9$ ;  $-P^{\dagger}R^9R^{10}A^-$ ; or phenylene; and have one or more carbons replaced by -O.; -NR<sup>9</sup>-; -N<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A<sup>-</sup>-; -S.-; -SO.; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may wherein  $\mathbb{R}^9$ ,  $\mathbb{R}^{10}$ , and  $\mathbb{R}^w$  are independently selected from the group

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carboalkoxyalkyl; carboxyaryl; carboxyheterocyclyl; amino; alkylamino; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; carboxyalkylamino; alkoxyalkylamino; and acyl; and

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 $\mathbb{R}^3$ ,  $\mathbb{R}^4$ ,  $\mathbb{R}^{3A}$ , and  $\mathbb{R}^{4A}$  are independently selected from the group wherein A is a pharmaceutically acceptable anion; and

consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; and -SO<sub>3</sub>R<sup>9</sup>; or R<sup>3</sup> and R<sup>4</sup> together form =O; =NOR<sup>9</sup>; =S; =NNR<sup>9</sup>R<sup>10</sup>; =NR<sup>9</sup>; or

S

 $R^{3A}$  and  $R^{4A}$  together form =0; =NOR<sup>9</sup>; =S; =NNR<sup>9</sup>R<sup>10</sup>; =NR<sup>9</sup>; or

SS

consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; wherein  $\mathbb{R}^{11}$  and  $\mathbb{R}^{12}$  are independently selected from the group

cyanoalkyl; -OR2; -NR2R10; -SR2; -S(O)R2; -SO2R2; -SO3R2; -CO2R2; and carboalkoxyalkyl; cycloalkyl; cycloalkenyl; haloalkyl; hydroxyalkyl; -CONR<sup>9</sup>R<sup>10</sup>; or

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form a cyclic ring; and  $\mathbb{R}^{11}$  and  $\mathbb{R}^{12}$  together with the carbon atom to which they are attached

wherein R9 and R10 are as defined above; and

S heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>, SR<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -CO2R<sup>13</sup>; -OM; -SO2OM; -SO2NR<sup>13</sup>R<sup>14</sup>; -C(O)NR<sup>13</sup>R<sup>14</sup>; -C(O)OM; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary consisting of hydrogen; halogen; -CN; -NO2; oxo; alkyl; polyalkyl; haloalkyl; one or more  $R^{y}$  and  $R^{yA}$  are independently selected from the group

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OC(O)NR<sup>1</sup>R<sup>1</sup>, -NR<sup>1</sup>SOR<sup>1</sup>, -NR<sup>1</sup>SO<sub>R</sub>, -NR<sup>1</sup>SO<sub>R</sub>NR<sup>1</sup>SONR<sup>1</sup>R<sup>1</sup>, -PR<sup>13</sup>R<sup>14</sup>, -PR<sup>14</sup>, -PR<sup>13</sup>R<sup>14</sup>, -PR<sup>14</sup>,  $P(OR^{13})OR^{14}$ ; -S<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A<sup>-</sup>; and -N<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>-</sup>; and COR 13; -NR 13C(O)R 14; -NR 13C(O)NR 14R 15; -NR 13CO;R 14; -OC(O)R 15; -

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alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; -OR<sup>7</sup>; -NR<sup>7</sup>R<sup>8</sup>; -SR<sup>7</sup>; -S(O)R<sup>7</sup>; -SO<sub>2</sub>R<sup>7</sup>; -SO<sub>3</sub>R<sup>7</sup>; -CO<sub>2</sub>R<sup>7</sup>; -CO<sub>2</sub>R<sup>7</sup>; -CO<sub>2</sub>R<sup>7</sup>; -PR<sup>7</sup>R<sup>8</sup>; -N<sup>+</sup>R<sup>7</sup>R<sup>8</sup>R<sup>9</sup>A<sup>7</sup>; and heterocyclylalkyl, and polyether substituents of the RY and RYA radicals the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; optionally may be further substituted with one or more radicals selected from alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl

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-; -S-; -SO-; -SO<sub>2</sub>-; -S<sup>†</sup>R<sup>7</sup>A-; -PR<sup>7</sup>-; -P(O)R<sup>7</sup>-; -P<sup>†</sup>R<sup>7</sup>R<sup>8</sup>A-; or phenylene; optionally may have one or more carbons replaced by -O-; -NR -; -N+R 7R 8Aalkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the RY and RYA radicals wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl

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P(O)(OR<sup>7</sup>)OR<sup>8</sup>; and

જ 8 consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; wherein  $\mathbb{R}^{13}$ ,  $\mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  are independently selected from the group wherein  $\mathbb{R}^7$  and  $\mathbb{R}^8$  are independently selected from the group

with one or more radicals selected from the group consisting of oxo, carboxy, attached form a mono- or polycyclic heterocyclyl that is optionally substituted alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; wherein R13 and R14 together with the nitrogen atom to which they are

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and quaternary salts; or

wherein  $\mathbb{R}^{14}$  and  $\mathbb{R}^{15}$  together with the nitrogen atom to which they are

alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; attached form a cyclic ring; and wherein the R <sup>13</sup>, R <sup>14</sup>, and R <sup>15</sup> alkyl; haloalkyl; cycloalkyl; polyalkyl;

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radicals optionally may be substituted with one or more radicals selected from alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether hydroxyalkyl; suifoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl;

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heterocyclyl, quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl;  $-OR^{16}$ ;  $-NR^9R^{10}$ ;  $-N^*R^9R^{11}R^{12}A^-$ ;  $-SR^{16}$ ;  $-S(O)R^2$ ;  $-SO_2R^9$ ;  $-SO_3R^{16}$ ; CO2R 16; -CONR 9R 10; -SO2NR 9R 10; -PO(OR 16)OR 17; -PR 9R 10; P+R9R10R11A-; -S+R9R10A-; and carbohydrate residue; and Ξ

wherein the R  $^{13},$  R  $^{14},$  and R  $^{15}$  alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl;

N+R9R10A: .5: .50:, .502:, .5+R9x:, .PR9:, .P+R9R10A:; .P(0)R9.; radicals optionally may have one or more carbons replaced by -O-; -NR9-; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and 120

wherein R 16 and R 17 are independently selected from the group consisting of R9 and M; and 125

wherein M is a pharmaceutically acceptable cation; and wherein n is 0, 1 or 2; and

 $R^{N}$  and  $R^{\text{MA}}$  are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aralkyl; and heterocyclylalkyl; and wherein R9, R10, R11, R12, RW, and A are as defined above; and 23

 $OR^{13}$ ;  $\cdot NR^{13}R^{14}$ ;  $\cdot SR^{13}$ ;  $\cdot S(O)R^{13}$ ;  $\cdot S(O)R^{13}$ ;  $\cdot SO_3R^{13}$ ;  $\cdot S^{\dagger}R^{13}R^{14}A_{+}$ ;  $\cdot$ one or more RX and RXA radicals are independently selected from the  ${
m NR}^{13} {
m OR}^{14}$ ; - ${
m NR}^{13} {
m NR}^{14} {
m R}^{15}$ ; - ${
m CO}_2 {
m R}^{13}$ ; - ${
m OM}$ ; - ${
m SO}_2 {
m OM}$ ; - ${
m SO}_2 {
m NR}^{13} {
m R}^{14}$ ; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether, acyloxy; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; group consisting of hydrogen; halogen; -CN; -NO2; alkyl; cycloalkyl; 135

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 $\mathrm{p}^{+}\mathrm{R}^{\,13}\mathrm{R}^{\,14}\mathrm{R}^{\,15}\mathrm{A}^{\,;}$  amino acid residue; peptide residue; and carbohydrate residue; 5

-NR9R10; -N+R9R10RWA; -SR16; -S(O)R9; -SO2R9; -SO3R16; -CO2R16; more radicals selected from the group consisting of halogen; -CN; oxo; -OR 16, hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; CONR9R10, -SO2NR9R10, -PO(OR19)OR17, -PR9R10, -P+R9R11R12A-; . polyether; acyloxy radicals optionally may be further substituted with one or wherein the RX and RXA alkyl; cycloalkyl; polyalkyl; haloalkyl; S+R9R10A; and carbohydrate residue; and 145

hydroxyalkyl; alkenyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether;  $-OR^{13}$ ;  $-NR^{13}R^{14}$ ;  $-SR^{13}$ ;  $-S(O)R^{13}$ ;  $-SO_2R^{13}$ ;  $-SO_3R^{13}$ ; . wherein the RX and RXA quaternary heterocyclyl radical optionally may be substituted with one or more radicals selected from the group consisting of NR <sup>13</sup> OR <sup>14</sup>; -NR <sup>13</sup> NR <sup>14</sup>R <sup>15</sup>; -CO<sub>2</sub>R <sup>13</sup>; OM; -SO<sub>2</sub>OM; -SO<sub>2</sub>NR <sup>13</sup>R <sup>14</sup>; halogen; -CN; -NO2; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl; 150

C(O)NR<sup>13</sup>R<sup>14</sup>,-C(O)OM; -COR<sup>13</sup>,-P(O)R<sup>13</sup>R<sup>14</sup>;-PR<sup>13</sup>R<sup>14</sup>;-P<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A;-P(OR<sup>13</sup>)OR<sup>14</sup>;-S<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A;-N<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A;and carbohydrate residue; and 155

have one or more carbons replaced by -O-; -NR<sup>13</sup>; -N<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A-; -S-; -SO-; acid; peptide; polypeptide; carbohydrate; polyether; or polyalkyl; wherein said carbohydrate residue; and polyalkyl optionally may have one or more carbons replaced by -O-; -NR<sup>9</sup>-; -N<sup>+</sup>R<sup>9</sup>R <sup>10</sup>A<sup>-</sup>-; -S-; -SO-; -SO<sub>2</sub>-; -S<sup>+</sup>R<sup>9</sup>A--; -PR<sup>9</sup>-; --SO2-; -S<sup>+</sup>R<sup>13</sup>A<sup>-</sup>-; -PR<sup>13</sup>-; -P(O)R<sup>13</sup>-; -P<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A<sup>-</sup>-; phenylene; amino wherein the  $\boldsymbol{R}^{\boldsymbol{X}}$  and  $\boldsymbol{R}^{\boldsymbol{X}\boldsymbol{A}}$  radicals comprising carbon optionally may phenylene; amino acid residue; peptide residue; polypeptide residue; P+R9R10A-; or -P(O)R9-; and 9

wherein R 18 is selected from the group consisting of alkyl; alkenyl; heterocyclylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and alkynyl; aryl; heterocyclyl; quatemary heterocyclyl; arylalkyl;

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halogen; -CN; NO; oxo; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N<sup>+</sup>R<sup>9</sup>R<sup>11</sup>R<sup>12</sup>A<sup>-</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; be substituted with one or more radicals selected from the group consisting of arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl radicals optionally may wherein the R11 alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl;

 $-SO_2R^9; -SO_3R^9; -CO_2R^9; -CONR^9R^{10}; -SO_2OM; -SO_2NR^9R^{10}; -PR^9R^{10}; -P(OR^{16})OR^{17}; -PO(OR^{16})OR^{17}; and -C(O)OM; and$ 

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defined above; and wherein R?, R10, R11, R12, R13, R14, R15, R16, R17, R\*, A7, and M are as

80 alkyne diyl; polyalkane diyl; alkoxy diyl; polyether diyl; polyalkoxy diyl; polypeptide residue; can optionally have one or more carbons replaced by -O-; polyalkoxy diyl; carbohydrate residue; amino acid residue; peptide residue; and alkene diyl; alkyne diyl; polyalkane diyl; alkoxy diyl; polyether diyl; carbohydrate; amino acid; and peptide; polypeptide; wherein alkane diyl; R19 is selected from the group consisting of alkane diyl; alkene diyl

185 PTR 'R'A:; phenylene; heterocyclyl; quaternary heterocyclyl; or aryl;  $-NR^{7}_{-1},N^{\dagger}R^{7}R^{8}A \cdot \cdot ,-S \cdot ;-SO \cdot ,-SO _{2}\cdot ,-S^{\dagger}R^{\prime}A \cdot \cdot ,-PR^{\prime}\cdot ,-P(O)R^{\prime}\cdot ;$ wherein alkane diyl; alkene diyl; alkyne diyl; polyalkane diyl; alkoxy

diyl; polyether diyl; polyalkoxy diyl; carbohydrate residue; amino acid residue;

190 arylalkyl; halogen; oxo; -OR <sup>13</sup>; -NR <sup>13</sup>R <sup>14</sup>; -SR <sup>13</sup>; -S(O)R <sup>13</sup>; -SO<sub>2</sub>R <sup>13</sup>; -SO<sub>3</sub>R <sup>13</sup>; -NR <sup>13</sup>OR <sup>14</sup>; -NR <sup>13</sup>NR <sup>14</sup>R <sup>15</sup>; -NO<sub>2</sub>; -CO<sub>2</sub>R <sup>13</sup>; -CN; -OM; substituent groups independently selected from the group consisting of alkyl; alkenyi; alkynyi; polyalkyi; polyether; aryi; haloalkyi; cycloalkyi; heterocyclyi; peptide residue; and polypeptide residue can be substituted with one or more

SO<sub>2</sub>OM; -SO<sub>2</sub>NR <sup>13</sup>R <sup>14</sup>; -C(O)NR <sup>13</sup>R <sup>14</sup>; -C(O)OM; -COR <sup>13</sup>; -P(O)R <sup>13</sup>R <sup>14</sup>; -PR <sup>13</sup>R <sup>14</sup>; -P <sup>†</sup>R <sup>13</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>15</sup>A; -P(OR <sup>13</sup>)OR <sup>15</sup>; -S<sup>\*</sup>R <sup>15</sup>R <sup>14</sup>A; and -P(O)R <sup>13</sup>R <sup>14</sup>; -PR <sup>13</sup>R <sup>14</sup>A; and -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>13</sup>R <sup>14</sup>A; -P(O)R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R <sup>14</sup>R

wherein R?, R4, R11, R12, R13, R14 R13, and A are as defined above; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

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- independently selected from the group consisting of hydrogen and alkyl. A compound of claim 121 wherein R<sup>1</sup>, R<sup>1</sup>, R<sup>2</sup>, and R<sup>2</sup> are
- independently selected from the group consisting of hydrogen and  $C_i$ - $C_{10}$  alkyl. A compound of claim 121 wherein R<sup>1</sup>, R<sup>1</sup>, R<sup>2</sup>, and R<sup>2</sup> are
- independently selected from the group consisting of C2-C7 alkyl. A compound of claim 121 wherein R<sup>1</sup>, R<sup>1</sup>, R<sup>2</sup>, and R<sup>2</sup> are

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- independently selected from the group consisting of C2-C4 alkyl. A compound of claim 121 wherein R1, R14, R2, and R24 are
- and isobutyl. independently selected from the group consisting of ethyl; n-propyl; n-butyl; 126. A compound of claim 121 wherein R1, R14, R2, and R24 are
- wherein R<sup>9</sup> is as defined in claim 121. independently selected from the group consisting of hydrogen and -OR, 127. A compound of claim 121 wherein R3, R3A, R4, and R4A are
- A compound of claim 126 wherein R° is hydrogen.
- independently selected from the group consisting of hydrogen, alkyl and 129. A compound of claim 121 wherein R<sup>N</sup> and R<sup>NA</sup> are
- and  $aryl(C_1-C_{10})alkyl$ . independently selected from the group consisting of hydrogen, (C<sub>1</sub>-C<sub>10</sub>)alkyl 130. A compound of claim 121 wherein R<sup>N</sup> and R<sup>NA</sup> are
- and benzyl. independently selected from the group consisting of hydrogen, methyl, ethyl 131. A compound of claim 121 wherein R<sup>N</sup> and R<sup>NA</sup> are
- dimethylamino. independently selected from the group consisting of methoxy and 132. A compound of claim 121 wherein one or more Rx and RxA are
- 133. A compound of claim 121 wherein q and r are each 1.
- hydroxy; -NO2; (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; independently selected from selected from the group consisting of halogen; 134. A compound of claim 121 wherein one or more Ry are

heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; polyether, -OR<sup>13</sup>;-NR<sup>13</sup>R<sup>14</sup>; and -NR<sup>13</sup>C(O)R<sup>14</sup>;

wherein  $R^{13},\,R^{14},\,{\rm and}\,\,R^{15}$  are independently selected from the group quaternary heterocyclyl(C1-C10)alkyl; (C1-C10)alkylheterocyclyl(C1-C10)alkyl; consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; haloC<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C1-C10)alkylammonium(C1-C10)alkyl; and polyether; or

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C<sub>10</sub>)alkyi; quaternary heterocyclyi(C<sub>1</sub>-C<sub>10</sub>)alkyi; (C<sub>1</sub>-C<sub>10</sub>)alkylheterocyclyi(C<sub>1</sub>heterocyclyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>optionally may be substituted with one or more radicals selected from the heterocyclyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy; carboxy(C<sub>1</sub>wherein the  $R^{13},\,R^{14},\,$  and  $R^{15}\,(C_{\rm l}\text{-}C_{\rm lo})$  alkyl; halo(C\_{-}C\_{\rm lo}) alkyl; C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether radicals Cio, alkyl; -OR 16; -NR9R10; -N\*R9R10RWA; and -CONR9R10; and group consisting of halogen; (C1-C10)alkyl; heterocyclyl; quatemary

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consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; ammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; wherein  $\rm R^9$  ,  $\rm R^{10}$  and  $\rm R^{W}$  are independently selected from the group  $(C_{i}\text{-}C_{i0}) alkylammonium (C_{i}\text{-}C_{i0}) alkyl; \ aryl (C_{i}\text{-}C_{i0}) alkyl; \ heterocyclyl (C_{i}\text{-}C_{i0}) alkyl ammonium (C_{i}\text{-}C_{i0}) alkyl; \ heterocyclyl (C_{i}\text{-}C_{i0}) alkyl ammonium (C_{i}\text{-}C_{i0}) a$ C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; carbo(C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxyheterocyclyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkylamino; and acyl; and wherein A is a pharmaceutically acceptable anion; and 8

 $\mathbb{R}^{11}$  and  $\mathbb{R}^{12}$  together with the carbon atom to which they are attached wherein  $R^{1\, 1}$  and  $R^{1\, 2}$  are independently selected from the group consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; and carbo(C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; or 23

form a cyclic ring; wherein  $R^{16}$  and  $R^{17}$  are independently selected from the group consisting of R<sup>9</sup> and M; and 8

wherein M is a pharmaceutically acceptable cation.

diyl; wherein alkane diyl and polyalkane diyl can optionally have one or more carbons replaced by -O-; -NR<sup>7</sup>-; -N<sup>+</sup>R<sup>7</sup>R<sup>8</sup>A-; -S.; -SO-; -SO<sub>2</sub>-; -S<sup>+</sup>R<sup>7</sup>A-; group consisting of alkane diyl; polyalkane diyl; alkoxy diyl; and polyalkoxy 135. A compound of claim 121 wherein R19 is selected from the

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PR7.; -P(O)R7.; -P\*R7R8A.; or phenylene, wherein R1 and R1 are defined as in claim 121.

carbons are optionally replaced by -O-; -NR 7-; -N+R 7R 8-; -SO-; -SO2-; -S<sup>+</sup>R<sup>7</sup>A--; -PR<sup>7</sup>-; -P(O)R<sup>7</sup>-; -P<sup>+</sup>R<sup>7</sup>R<sup>8</sup>A--; phenylene; amino acid residue; A compound of claim 121 wherein R19 is selected from the group consisting of alkoxy diyl and polyalkoxydiyl wherein one or more peptide residue; polypeptide residue; carbohydrate residue; or polyalkyl, wherein R9 and R10 are defined as in claim 121.

137. A compound of claim 121 having the structural formula:

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A compound of formula (V):

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wherein :

q is an integer from 0 to 4;

r is an integer from 0 to 3;

u is an integer from 0 to 5; t is an integer from 0 to 4;

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alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; consisting of hydrogen; alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl;  $R^1, R^2, R^{1A}$ , and  $R^{2A}$  are independently selected from the group

and (polyalkyl)aryl; or heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl;  $\mathbb{R}^1$  and  $\mathbb{R}^2$  taken together with the carbon to which they are attached

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form C3-C10 cycloalkyl or C3-C10 cycloalkenyl; form  $C_3\text{-}C_{10}$  cycloalkyl or  $C_3\text{-}C_{10}$  cycloalkenyl; or  $R^{1A}$  and  $R^{2A}$  taken together with the carbon to which they are attached

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aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; wherein the R<sup>1</sup>, R<sup>2</sup>, R<sup>1A</sup>, and R<sup>2A</sup> alkyl; cycloalkyl; alkenyl

heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may CN; halogen; oxo; -OR9; -NR9R10; -N+R9R10RWA; -SR9; -S+R9R10A; be substituted with one or more radicals selected from the group consisting of

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CONR<sup>9</sup>R<sup>10</sup>; and P+R9R10RWA;-PR9R10;-S(O)R9;-SO2R9;-SO3R9;-CO2R9; and

8 alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; wherein the  $R^1$ ,  $R^2$ ,  $R^{1A}$ , and  $R^{2A}$  alkyl; cycloalkyl; alkenyl;

3 have one or more carbons replaced by -O-; -NR 9-; -N+R 9R 10A-; -S-; -SO-; -SO2-; -STR'A-; -PR'-; -P(O)R'-; -PTR'R'I'A-; or phenylene; and heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may wherein  $\mathbb{R}^9$ ,  $\mathbb{R}^{10}$ , and  $\mathbb{R}^w$  are independently selected from the group

carboalkoxyalkyl; carboxyaryl; carboxyheterocyclyl; amino; alkylamino; consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl carboxyalkylamino; alkoxyalkylamino; and acyl; and

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wherein A is a pharmaceutically acceptable anion; and

consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; -OR<sup>9</sup>; -NR<sup>9</sup>R<sup>10</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; and -SO<sub>3</sub>R<sup>9</sup>; or  $R^3$ ,  $R^4$ ,  $R^{3A}$ , and  $R^{4A}$  are independently selected from the group

S  $=CR^{11}R^{12}$ R3 and R4 together form =O; =NOR9; =S; =NNR9R10; =NR9; or

-CR11R12; R<sup>3A</sup> and R<sup>4A</sup> together form =O; =NOR<sup>9</sup>; =S; =NNR<sup>9</sup>R<sup>10</sup>; =NR<sup>9</sup>; or

S 8 -CONR<sup>9</sup>R<sup>10</sup>; or carboalkoyyalkyl; cycloalkyl; cycloalkenyl; haloalkyl; hydroxyalkyl; cyanoalkyl; -OR<sup>9</sup>; -NR<sup>9</sup>R <sup>10</sup>; -SR<sup>9</sup>; -S(O)R<sup>9</sup>; -SO<sub>2</sub>R<sup>9</sup>; -SO<sub>3</sub>R<sup>9</sup>; -CO<sub>2</sub>R<sup>9</sup>; and heterocyclyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkynyl; aryl; wherein  $\mathbb{R}^{11}$  and  $\mathbb{R}^{12}$  are independently selected from the group

form a cyclic ring; and  $\mathbb{R}^{11}$  and  $\mathbb{R}^{12}$  together with the carbon atom to which they are attached

wherein R<sup>9</sup> and R<sup>10</sup> are as defined above; and

consisting of halogen; -CN; -NO2; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary one or more  $R^{y}$  and  $R^{yA}$  are independently selected from the group

heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>

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SR<sup>13</sup>;-S(O)R<sup>13</sup>;-SO<sub>2</sub>R<sup>13</sup>;-SO<sub>3</sub>R<sup>13</sup>;-NR<sup>13</sup>OR<sup>14</sup>;-NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>;-CO2R<sup>13</sup>; -OM; -SO2OM; -SO2NR<sup>13</sup>R<sup>14</sup>; -C(0)NR<sup>13</sup>R<sup>14</sup>; -C(0)OM; COR<sup>13</sup>; -NR<sup>13</sup>C(O)R<sup>14</sup>; -NR<sup>13</sup>C(O)NR<sup>14</sup>R<sup>15</sup>; -NR<sup>13</sup>CO<sub>2</sub>R<sup>14</sup>; -OC(O)R<sup>13</sup>; OC(O)NR<sup>19</sup>R"; -NR<sup>11</sup>SOR", -NR<sup>11</sup>SO<sub>1</sub>R", -NR<sup>11</sup>SONR'R"; -NR<sup>11</sup>SO<sub>1</sub>NR'R"; -P(O)R<sup>13</sup>R<sup>14</sup>, -PR<sup>13</sup>R<sup>14</sup>, -P<sup>\*</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A<sup>\*</sup>; -P(OR13)OR14; -S+R13R14A; and -N+R13R14R15A; and

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the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; optionally may be further substituted with one or more radicals selected from heterocyclyl;  $-OR_7'$ :  $-NR^7R^8$ ;  $-SR^7$ ;  $-S(O)R^7$ ;  $-SO_2R^7$ ;  $-SO_3R^7$ ;  $-SO_3R^7$ ;  $-SO_3R^7$ ;  $-SO_3R^7$ ;  $-SO_3R^8$ ;  $-PR^7R^8$ ;  $-PR^8$ ; wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, heterocyclylalkyl, and polyether substituents of the RY and RYA radicals alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quatemary P(O)(OR')OR'; and 8

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optionally may have one or more carbons replaced by -0-; -NR7.; -N+R7R8A. : -S-; -SO-; -SO2-; -S<sup>\*</sup>R<sup>7</sup>A-; -PR<sup>7</sup>-; -P(O)R<sup>7</sup>-; -P<sup>\*</sup>R<sup>7</sup>R<sup>8</sup>A-; or phenylene; wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, heterocyclylalkyl, and polyether substituents of the RY and RYA radicals alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, ᇤ

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wherein  $\mathbb{R}^{13}, \mathbb{R}^{14}$ , and  $\mathbb{R}^{15}$  are independently selected from the group consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; wherein  $\mathbb{R}^7$  and  $\mathbb{R}^8$  are independently selected from the group heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; 23

wherein R13 and R14 together with the nitrogen atom to which they are alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or attached form a mono- or polycyclic heterocycly! that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl;

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wherein R<sup>14</sup> and R<sup>15</sup> together with the nitrogen atom to which they are attached form a cyclic ring; and

and quaternary salts; or

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wherein the  $R^{13},\,R^{14},\,$  and  $R^{15}$  alkyl, haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quatemary heterocyclyl; arylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl;

radicals optionally may be substituted with one or more radicals selected from alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl;

heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; OR<sup>16</sup>; NR<sup>9</sup>R<sup>10</sup>; NR<sup>9</sup>R<sup>16</sup>; S(O)R<sup>2</sup>; SO<sub>2</sub>R<sup>2</sup>; SO<sub>3</sub>R<sup>16</sup>; hydroxyalkyi; sulfoalkyi; alkenyi; alkynyi; aryi; heterocyclyi; quaternary  $\cos^{16}$  .  $\cos^{9}$  R $^{10}$  , - $\sin^{9}$  R $^{10}$  . PO(OR $^{16}$ )OR $^{17}$  . PR $^{9}$ R $^{10}$  $P^{+}R^{9}R^{10}R^{11}A^{-}, \cdot S^{+}R^{9}R^{10}A^{-};$  and carbohydrate residue; and 

wherein the  $R^{13}, R^{14},$  and  $R^{15}$  alkyl; haloalkyl; cycloalkyl; polyalkyl; N+R9R10A: -S.; -SO; -SO; -S<sup>\*</sup>R9A:; -PR9:; -P+R9R10A:; -P(O)R9:; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; -NR2-; phenylene; carbohydrate residue; amino acid residue; peptide residue; or alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; 120 125

wherein R 16 and R 17 are independently selected from the group consisting of R9 and M; and polypeptide residue; and 130

wherein R, R10, R11, R12, RW and A are as defined above; and wherein M is a pharmaceutically acceptable cation; and wherein n is 0, 1 or 2; and

one or more RX and RXA radicals are independently selected from the  $R^{N}$  and  $R^{\mathsf{MA}}$  are independently selected from the group consisting of polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; group consisting of hydrogen; halogen; -CN; -NO2; alkyl; cycloalkyl; hydrogen; alkyl; alkenyl; alkynyl; aralkyl; and heterocyclylalkyl; and 135

 ${\sf NR^{1C}(O)R^{13}; -C(O)NR^{13}R^{14}; -C(O)OM; -COR^{13}; -OR^{18}; -S(O)_{\rm DNR^{13}R^{14}}}$ NR <sup>13</sup> OR <sup>14</sup>; -NR <sup>13</sup> NR <sup>14</sup>R <sup>15</sup>; -CO<sub>2</sub>R <sup>13</sup>; -OM; -SO<sub>2</sub> OM; -SO<sub>2</sub> NR <sup>13</sup>R <sup>14</sup>; quatemary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy.-OR <sup>13</sup>, -NR <sup>13</sup>R <sup>14</sup>, -SR <sup>13</sup>, -S(O)R <sup>13</sup>, -S(O)R <sup>13</sup>, -SO<sub>3</sub>R <sup>13</sup>, -S<sup>+</sup>R <sup>13</sup>R <sup>14</sup>, 5

and carbohydrate residue;  $\mathrm{p^+R^{13}R^{14}R^{15}A^-}$ ; amino acid residue; peptide residue; polypeptide residue; -NR 13R 18; -NR 18OR 14; -N+R 13R 14R 15A; -PR 13R 14; -P(O)R 13R 14; -

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150 S<sup>+</sup>R<sup>9</sup>R<sup>10</sup>A<sup>-</sup>; and carbohydrate residue; and CONR 9R 10; -SO2NR 9R 10; -PO(OR 19)OR 17; -PR 9R 10; -P+R 9R 11R 12A; --NR9R10; N+R9R10RWA; -SR16; -S(O)R9; -SO2R9; -SO3R16; -CO2R16 more radicals selected from the group consisting of halogen; -CN; oxo; -OR 16, hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy radicals optionally may be further substituted with one or wherein the RX and RX alkyl; cycloalkyl; polyalkyl; haloalkyl;

polyether; -OR 13; -NR 13R 14; -SR 13; -S(O)R 13; -SO2R 13; -SO3R 13; halogen; -CN; -NO2; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl; NR 13 OR 14; -NR 13 NR 14R 15; -CO2R 13; OM; -SO2OM; -SO2NR 13R 14; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; be substituted with one or more radicals selected from the group consisting of wherein the RX and RXA quaternary heterocyclyl radical optionally may

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6 C(0)NR<sup>13</sup>R<sup>14</sup>; -C(0)OM; -COR<sup>13</sup>; -P(0)R<sup>13</sup>R<sup>14</sup>, -PR<sup>13</sup>R<sup>14</sup>; -PR<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A; and P<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A; -P(0R<sup>13</sup>)OR<sup>14</sup>; -S<sup>+</sup>R<sup>13</sup>R<sup>14</sup>A; -N<sup>+</sup>R<sup>13</sup>R<sup>14</sup>R<sup>15</sup>A; and carbohydrate residue; and

or polyalkyl; wherein said phenylene; amino acid residue; peptide residue;  $-S^{\dagger}R^{9}A$ :;  $-PR^{9}$ ;  $-P^{\dagger}R^{9}R^{10}A$ :; or  $-P(O)R^{9}$ -; and one or more carbons replaced by -O-; -NR<sup>9</sup>-; -N<sup>†</sup>R<sup>9</sup>R<sup>10</sup>A<sup>-</sup>-; -S-; -SO-; -SO<sub>2</sub>polypeptide residue; carbohydrate residue; and polyalkyl optionally may have residue; peptide residue; polypeptide residue; carbohydrate residue; polyether, wherein the  $R^X$  and  $R^{X_i}$  radicals comprising carbon optionally may have one or more carbons replaced by -O-; -NR <sup>13</sup>; -N<sup>+</sup>R <sup>13</sup>R <sup>14</sup>A-; -S-; -SO-; -S<sup>+</sup>R <sup>13</sup>A<sup>-</sup>; -PR <sup>13</sup>; -P(O)R <sup>13</sup>; -P<sup>+</sup>R <sup>13</sup>R <sup>14</sup>A-; phenylene; amino acid

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heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; wherein  $\mathbb{R}^{18}$  is selected from the group consisting of alkyl; alkenyl;

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heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; be substituted with one or more radicals selected from the group consisting of arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl radicals optionally may wherein the R 18 alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary

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8 halogen; -CN; NO;; oxo;  $-OR^9$ ;  $-NR^9R^{10}$ ;  $-N^+R^9R^{11}R^{12}A$ ;  $-SR^9$ ;  $-S(O)R^9$ ;  $-SO_2R^9$ ;  $-SO_2R^9$ ;  $-CO_2R^9$ ;  $-CONR^9R^{10}$ ;  $-SO_2OM$ ;  $-SO_2NR^9R^{10}$ ;  $-PR^9R^{10}$ ;  $-P(OR^{16})OR^{17}$ ;  $-PO(OR^{16})OR^{17}$ ; and -C(O)OM; and

wherein R9, R10, R11, R12, R13, R14, R15, R16, R17, Rw, A, and M are as

peptide residue; and polypeptide residue; can optionally have one or more carbohydrate residue; amino acid residue; peptide residue; and polypeptide carbons replaced by -O-; -NR '-; -NTR 'R 'A-; -S-; -SO-; -SO2-; -STR 'A-; diyl; polyether diyl; polyalkoxy diyl; carbohydrate residue; amino acid residue; residue; wherein alkane diyl; alkene diyl; alkyne diyl; polyalkane diyl; alkoxy alkyne diyl; polyalkane diyl; alkoxy diyl; polyether diyl; polyalkoxy diyl; R<sup>19</sup> is selected from the group consisting of alkane diyl; alkene diyl;

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9 PR<sup>7</sup>-; -P(O)R<sup>7</sup>-; -P<sup>+</sup>R<sup>7</sup>R<sup>8</sup>A·-; phenylene; heterocyclyl; quaternary heterocyclyl; or aryl;

peptide; and polypeptide residue can be substituted with one or more diyl; polyether diyl; polyalkoxy diyl; carbohydrate residue; amino acid residue; wherein alkane diyl; alkene diyl; alkyne diyl; polyalkane diyl; alkoxy

200 195 arylalkyl; halogen; oxo; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; -SR<sup>13</sup>; -S(O)R<sup>13</sup>; -SO<sub>2</sub>R<sup>13</sup>; -SO<sub>3</sub>R<sup>13</sup>; -NR<sup>13</sup>OR<sup>14</sup>; -NR<sup>13</sup>NR<sup>14</sup>R<sup>15</sup>; -NO<sub>2</sub>; -CO<sub>2</sub>R<sup>13</sup>; -CN; -OM; alkenyl; alkynyl; polyalkyl; polyether; aryl; haloalkyl; cycloalkyl; heterocyclyl; substituent groups independently selected from the group consisting of alkyl;

a pharmaceutically acceptable salt, solvate, or prodrug thereof. wherein R?, R1, R11, R12, R14, R15, and A are as defined above; or

- independently selected from the group consisting of hydrogen and alkyl 139. A compound of claim 138 wherein R<sup>1</sup>, R<sup>1</sup>A, R<sup>2</sup>, and R<sup>2</sup>A are
- independently selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>10</sub> alkyl 140. A compound of claim 138 wherein R', R', R2, and R2 are
- independently selected from the group consisting of  $C_2$ - $C_7$  alkyl 141. A compound of claim 138 wherein R1, R14, R2, and R24 are

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142. A compound of claim 138 wherein R¹, R¹, and R²a are independently selected from the group consisting of C₂-C₄ alkyl.

- 143. A compound of claim 138 wherein R¹, R¹A, R³, and R²A are independently selected from the group consisting of ethyl; n-propyl; n-butyl; and isobutyl.
- 144. A compound of claim 138 wherein R<sup>3</sup>, R<sup>3</sup>, R<sup>4</sup>, and R<sup>4</sup>A are independently selected from the group consisting of hydrogen and -OR\*, wherein R<sup>9</sup> is as defined in claim 138.
- 145. A compound of claim 144 wherein R9 is hydrogen.
- 146. A compound of claim 138 wherein  $\mathbb{R}^N$  and  $\mathbb{R}^{NA}$  are independently selected from the group consisting of hydrogen, alkyl and aralkyl.
- 147 A compound of claim 138 wherein  $R^N$  and  $R^{NA}$  are independently selected from the group consisting of hydrogen,  $(C_1-C_{10})$ alkyl and aryl $(C_1-C_{10})$ alkyl.
- 148. A compound of claim 138 wherein R<sup>N</sup> and R<sup>MA</sup> are independently selected from the group consisting of hydrogen, methyl, ethyl and benzyl.
- 149. A compound of claim 138 wherein one or more  $R^{\star}$  and  $R^{\star A}$  are independently selected from the group consisting of methoxy and dimethylamino.
- 150. A compound of claim 138 wherein q and r are each 1.
- 151. A compound of claim 138 wherein one or more R<sup>2</sup> are independently selected from selected from the group consisting of halogen; hydroxy; -NO2; (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl;

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beterocyclyl(C,-C<sub>io</sub>)alkyl; polyether; -OR<sup>13</sup>; -NR<sup>13</sup>R<sup>14</sup>; and -NR<sup>13</sup>C(O)R<sup>14</sup>;

wherein R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> are independently selected from the group consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkyl;

- (C<sub>1</sub>-C<sub>10</sub>)alkylammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; and polyether; or wherein the R<sup>13</sup>, R<sup>14</sup>, and R<sup>15</sup> (C<sub>1</sub>-C<sub>10</sub>)alkyl;halo(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl polyether radicals
  - 15 optionally may be substituted with one or more radicals selected from the group consisting of halogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; -OR<sup>16</sup>; -NR<sup>9</sup>R<sup>10</sup>; -N<sup>4</sup>R<sup>9</sup>R<sup>10</sup>R<sup>w</sup>A<sup>7</sup>; and -CONR<sup>9</sup>R<sup>10</sup>; and wherein R<sup>9</sup> and R<sup>10</sup> are independently selected from the group
- 20 consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; ammonium(C<sub>1</sub>-C<sub>10</sub>)alkyl; (C<sub>1</sub>-C<sub>10</sub>)alkyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxylcterocyclyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkylamino; and acyl; and wherein A is a pharmaceutically acceptable anion; and
- wherein R<sup>11</sup> and R<sup>12</sup> are independently selected from the group consisting of hydrogen; (C<sub>1</sub>-C<sub>10</sub>)alkyl; heterocyclyl; aryl(C<sub>1</sub>-C<sub>10</sub>)alkyl; carboxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; and carbo(C<sub>1</sub>-C<sub>10</sub>)alkoxy(C<sub>1</sub>-C<sub>10</sub>)alkyl; or R<sup>11</sup> and R<sup>12</sup> together with the carbon atom to which they are attached
  - form a cyclic ring; wherein  $\mathbb{R}^{15}$  and  $\mathbb{R}^{17}$  are independently selected from the group

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consisting of  $\mathbb{R}^9$  and M; and wherein M is a pharmaceutically acceptable cation.

152. A compound of claim 138 wherein R<sup>19</sup> is selected from the group consisting of alkane diyl; polyalkane diyl; alkoxy diyl; and polyalkane diyl; wherein alkane diyl and polyalkane diyl can optionally have one or more carbons replaced by -O-; -NR<sup>7</sup>; -N<sup>+</sup>R<sup>7</sup>R<sup>8</sup>A-; -SO-; -SO-; -SO<sub>2</sub>·· -S<sup>+</sup>R<sup>7</sup>A-; -

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 $PR^7$ :, -P(O)R <sup>7</sup>:, -P<sup>+</sup>R <sup>7</sup>R <sup>8</sup>A··; or phenylene, wherein R<sup>7</sup> and R<sup>8</sup> are defined as in claim 138.

153. A compound of claim 138 wherein R<sup>19</sup> is selected from the group consisting of alkoxy diyl and polyalkoxydiyl wherein one or more cairbons are optionally replaced by -O-; -NR<sup>7</sup>-; -N<sup>+</sup>R<sup>7</sup>R<sup>8</sup>A-; -S-; -SO-; -SO<sub>2</sub>-; -S<sup>+</sup>R<sup>7</sup>A-; -PR<sup>7</sup>-; -P(O)R<sup>7</sup>-; -P<sup>+</sup>R<sup>7</sup>R<sup>8</sup>A-; phenylene; amino acid; peptide; polypeptide; carbohydrate; or polyalkyl, wherein R<sup>9</sup> and R<sup>10</sup> are defined as in

## 154. A compound of claim 138 having the formula:

155. A pharmaceutical composition comprising an antihyperlipidemic effective amount of a compound of formula (I) of claim 1; and a pharmaceutically acceptable carrier.

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156. A pharmaceutical composition comprising an antiatherosclerotic effective amount of a compound of formula (I) of claim 1; and a pharmaceutically acceptable carrier.

157. A pharmaceutical composition comprising an antihypercholesterolemia effective amount of a compound of formula (I) of claim1; and

a pharmaceutically acceptable carrier.

- 158. A pharmaceutical composition comprising an antihyperlipidemic effective amount of a compound of formula (I) of claim 2; and a pharmaceutically acceptable carrier.
- 139. A pharmaceutical composition comprising an antiatherosclerotic effective amount of a compound of formula (I) of claim 2; and a pharmaceutically acceptable carrier.
- 160. A pharmaceutical composition comprising an antihypercholesterolemia effective amount of a compound of formula (I) of claim 2; and

a pharmaceutically acceptable carrier.

- 161. A method for the prophylaxis or treatment of a hyperlipidemic condition comprising administering to a patient in need thereof a composition of claim 155 in unit dosage form.
- 162 A method for the prophylaxis or treatment of an atherosclerotic condition comprising administering to a patient in need thereof a composition of claim 156 in unit dosage form.
- 163. A method for the prophylaxis or treatment of hypercholesterolemia comprising administering to a patient in need thereof a composition of claim 157 in unit dosage form.

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- condition comprising administering to a patient in need thereof a composition 164. A method for the prophylaxis or treatment of a hyperlipidemic of claim 158 in unit dosage form.
- A method for the prophylaxis or treatment of an atherosclerotic condition comprising administering to a patient in need thereof a composition of claim 159 in unit dosage form. 165.
- hypercholesterolemia comprising administering to a patient in need thereof a A method for the prophylaxis or treatment of composition of claim 160 in unit dosage form. 166

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Inventors; and

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- With international search report.

(88) Date of publication of the international search report: 14 December 2000 9) Inventors/Applicants (for US only); TOLLEFSON, (g Michael, B. [US/US]; 137 Big Hom Drive, Hainesville, IL 6030 (US), KOLLODZEJ, Steve, A. [US/US]; 2448 Carjon Road, Balbrin, MO 63021 (US), REITZ, David, A. B. [US/US]; 14814 Pleasant Ridge Court, Chesterfield, MO 63017 (US).

For two-letter codes and other abbreviation, refer to the "Guid-ance Notes on Codes and Abbreviation" appearing at the begin-ning of each regular issue of the PCT Gazette.

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(S) Title: 1.2-BENZOTHIAZEPINES FOR THE TREATMENT OF HYPERLIPDEMIC DISEASES
(S4) Title: 1.2-BENZOTHIAZEPINES FOR THE TREATMENT OF HYPERLIPDEMIC DISEASES
(S5) Abstract: Novel 1.1-dioxido-1.2-beauchtiatespines, derivatives and analogs thereof, pharmaceutical compositions containing them, and their use in medicine, particularly in the prophylaxia and/or treatment of hyperlipidemic diseases, conditions and/or disease, orders, such as those associated with atherosclerosis and/or hypertholesterolemia.

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### INTERNATIONAL SEARCH REPORT

PCT/US 00/02503

Name and mu	28	Date of the ac	'A' document consider to consider to consider to counter  X Furth		<b>→</b>	<b>&gt;</b>	>	Catagory *	EPO-Internal,	Documentatio	B. FIELDS SEARCHED MINIMUM documentation IPC 7 CO7D	IPC 7	A. CLASSIFI	
Name and mailing address of the ISA.  European Palest Office, P.B. 5818 Patenthan 2 NL 2200 IV Rilevik. Tal. (-3.770) 940-2501 Tz 31 611 epo nl. Fex: (-31-70) 940-25016	<b>July 2000</b>	Date of the actual completion of the international search	h is not metoral (s) or nother nother or	Further documents are listed in the continuation of box C.		WO 96 16051 A (WELLCOME FOUND ;BR LAWRENCE EDWARD (US); HANDLOW ANTI 30 May 1996 (1996-05-30) cited in the application claim 1	WO 98 02432 A (SUGIURA YOSHIHIRO ;DOI TAKAYUKI (JP); KATO KANEYOSHI (JP); KAWADA) 22 January 1998 (1998-01-22) cited in the application claim 8	WO 98 38182 A (GLAXO GROUP LTD ;HANDLON ANTHONY LOUIS (US); HUDGSON GORDON LEWIS) 3 September 1998 (1998-09-03) Formula (Ie) Claims 1,6	Citation of document, with indication, where appropriate, of the relevant passages	EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data	Occumentation searched other than minimum documentation to the extent that such documents are included in the fields searched of the control of the fields searched decimentation to the extent that such documents are included in the fields searched.	B. FELDS SEARCHED  Minimum documentation searched (citeatification system followed by desalification symbols)  IPC 7 C07D A61K	IPC 7 C07D281/02 A61K31/55 A61P3/06 C0 According to International Palant Chanaffestion (IPC) or to both national chanifestion and IPC	
Authorized officer Gettins, M	. 0 9. 08. 00	Date of mailing of the international search report	To last document published also the triamstonal filing data of profession out, and the published of profession of profession out to notifice with the application out to profession desired the profession desired the profession desired to profession of the profession of profession of profession of profession of profession of profession relevance; the database inventor as no market set plants the document of particular relevance; the database for document of profession of profession of profession of profession of profession of profession of profession of profession of profession of profession and profession of pro	Patent family members are listed in annex	-/	;BRIEADDY ANTHONY LOU)	; poi ); 22)	N LEWIS)	want pessages	a, CHEM ABS Data	uch documents are included in the fields so	n symbola)	C07D417/12	רכו/שט טט
	0	rch report	national filing data that applications but the applications but the applications but the applications but the applications but the applications but the applications but the applications but the application	n annex.		1-103	<b>.</b>	1-103	Relevant to claim No.		arched			00/02503

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Form PCT/ISA/210 (second sheet) (July 1992)

### INTERNATIONAL SEARCH REPORT

PCT/US 00/02503

C (Carelinus	C. (Continuation) DOCIMENTS CONSIDERED TO BE DELEVANT		2, 01000
Catagory *	Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.
~	WO 96 05188 A (WELLCOME FOUND ;BRIEADDY LAWRENCE EDWARD (US)) 22 February 1996 (1996-02-22) cited in the application claim 1		1-103
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page 2 of 2

#### INTERNATIONAL SEARCH REPORT

	<u>rotu</u>	Information on patent family member	r- q	<u> </u>	International A PCT/US 0	Application No 00/02503
Patent document clted in search report		Publication date		Patent family member(s)		Publication date
WO 9838182	∢	03-09-1998	₹	6823898	<b>A</b>	18-09-1998
WO 9802432	∢	22-01-1998	공능	3460797 10338672	44	09-02-1998 22-12-1998
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INTERNATIONAL SEARCH REPORT

International application No. PCT/US 00/02503

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)
This international Search Report has not been established in respect of certain claims under Article 17(2)(a) for the followerg reasons:
<ol> <li>X Caerns Nos.: Decause they relate to subject matter not required to be searched by this Authority, namely.</li> <li>Although claims 161-166 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.</li> </ol>
2 [X] Coarse Mea: 104-154 -all other claims only searched partially because they rete to part of the interestional Application that do not compy with the prescribed requiencents to each or stand that no meaningful fremational Search can be carried out, specifically: see FURTHER INFORMATION sheet PCT/ISA/210
Box is Coservations where unity of invention is lacking (Continuation of item 2 of first eheet) This international Searching Authority found multiple inventions in this international ancitation, as informer.
1. As all required additional search fees were timely paid by the applicant, this international Search Report covers all searchable claims.
2. The all searchable dains could be searched without effort justifying an additional lee, this Authority dig not invite payment of any additional lee.
<ol> <li>As only some of the required additional search less were timely paid by the applicant, this International Search Report covers only those datins for which less were paid, specifically claims Nos.</li> </ol>
4. The required additional search fees were timally paid by the explicent, Corsequently, this international Search Report is restricted to the Invention first mentioned in the cleims; it is covered by claims Nos.:
Remark on Probst  The additional search fres were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

Form PCTASA/210 (continuation of first sheet (1)) (July 1998)

International Application No. PCTUS 00 02503

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 104-154 -all other claims only searched partially

Present claims 1-166 relate to an extremely large number of possible compounds. In fact, the claims contain so many options, variables, possible permutations (e.g. prodrug), huge definitions (such as hydrocarbyl or containing at least one heteroatom) and provisos that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCI arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and/or concise), namely those compounds recited in the physically characterised and tested examples 1-24 on pages 284-327 and closely related homologous compounds as defined in the next paragraph. It is noted that only compounds of the examples of formulae (III). (IV) or (V). It should be noted that only examples which are clearly defined and physically characterised have been taken into consideration. Examples 101-1652 do not appear to be be defined as regards the RN substituent and are therefore not examples which are adequately defined for supporting the scope of the claims.

The search has been limited to the examples and a generalisation thereof to compounds of formula (I) in which R3 and R4 are H and OH, R5 is hydrogen and R6 is a (substituted) phenyl.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCI). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.